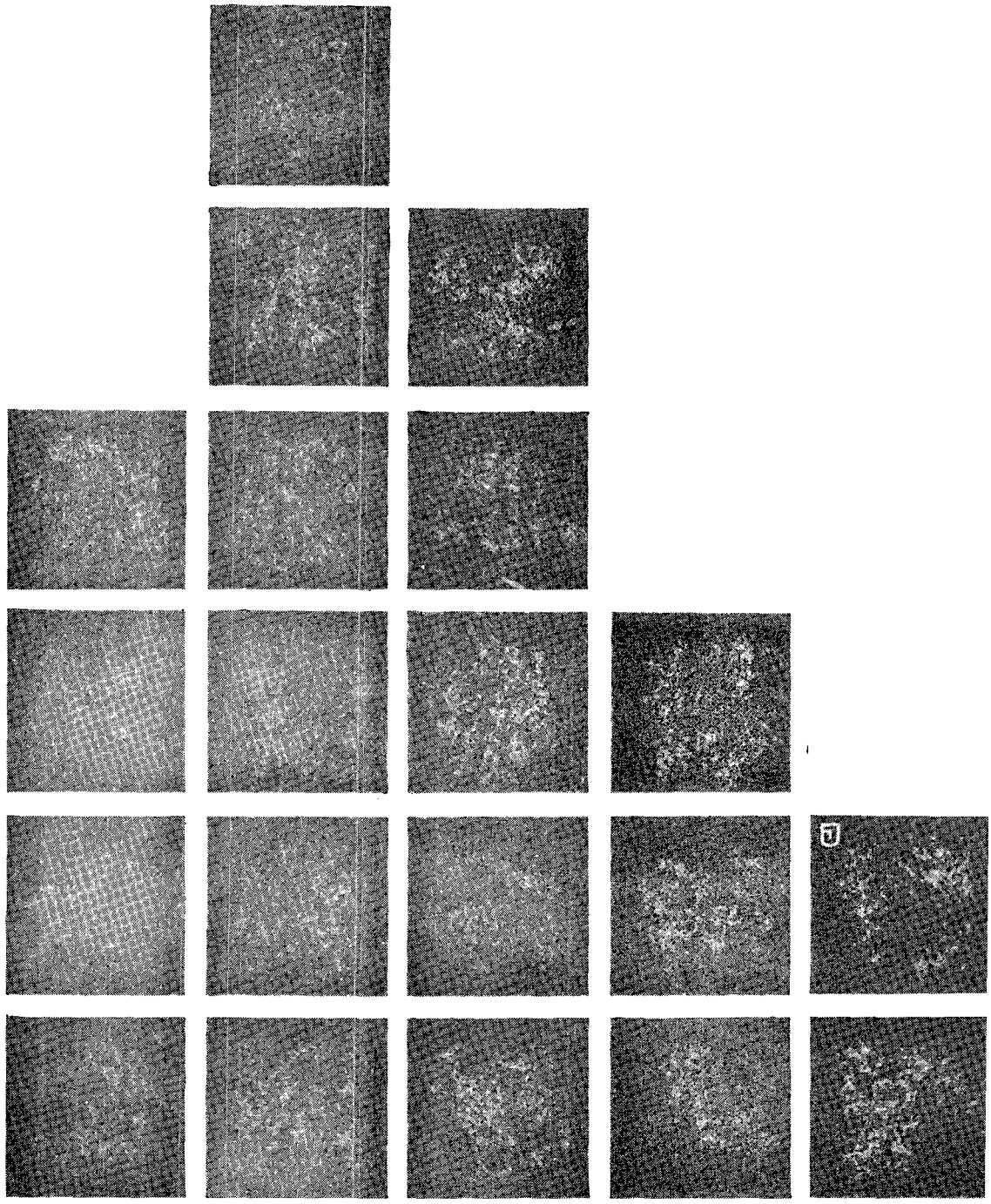
神経化学

VOL. 2 NO. 3 JUNE 1963



神 経 化 学 懇 話 会

—講　演—

脳組織のアミノ酸および蛋白質代謝の問題

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D. Richter (Director of Medical Research Council, Neuropsychiatric Research Unit) は4月の医学総会のために来日したが，4月17日午後，神経化学懇話会のために講演した。以下はその要約である。

今日の主題は脳のアミノ酸および蛋白質代謝の問題ですが，もっと広い立場からお話をしたいと思います。私どものResearch unit では基礎的な研究と精神病の臨床とが平行して行れていますが，これはお互の発展のために必要なことであると思れます。

さて，最初に脳の一般的の代謝のことを述べ，それとアミノ酸代謝との関連をのべることにしましょう。脳の代謝が活発なものであることはよく知られています。非常に沢山の酸素を消費して代謝しています。この代謝活性は大まかには脳の機能活動と関連しており，昏睡の場合には呼吸は低下し，一方アドレナリンを注射した場合やケイレンの場合には著しく昂進します。この活発なエネルギー代謝は殆ど悉くグルコースの酸化にもとづくものです。脂質やアミノ酸は血流中から利用されることは殆どありません。蛋白質の代謝はどうでしょうか。普通の常識としては，蛋白質の代謝は非常に不活発なものであると信じられていました。しかし，実際にS^{35}メチオニンを用いて脳の蛋白質の代謝回転をはかってみますと，意外に速やかなものであることがわかりました。脳の蛋白質の半減期は14日位で肝臓の蛋白質とほゞ同じです。ニューヨークのLajthaその他の研究者の成績も脳の蛋白質の代謝が活発なことを示しています。脳細胞のどの分画で蛋白代謝が活発であるかをみますと，ミクロゾーム分画，即ちリボゾームを含む分画で特に活発であることがわかりました。

脳ではなぜ蛋白代謝が活発なのでしょうか。まづ，脳のどこで活発な蛋白代謝が行れているのかが問題となります。大まかに言って灰白質では代謝回転は速やかで，白質ではおそいことが知られています。オートラジオグラフの方法を用いれば，やゝ詳しくしらべることができます。

結論としては，脳の部分によって蛋白代謝の非常に活発なところとそうでないところとがあることが明らかになったのですが，代謝活性はほゞ神経細胞の分布と一致したものであるようです。即ち，蛋白質代謝は神経細胞で活発に行れていると考えられています。

脳の蛋白質として，どのような蛋白質の代謝が活発であるのかと言う疑問もおこります。筋肉の場合のマイオシンのように機能的に意義のある蛋白質が脳にも存在するのでしょうか。S^{35}メチオニンを注射してから例えば3時間のちに脳をとって分画してみますと，放射能は殆どミクロゾーム分画に見出されます。特にリボ核蛋白の分画で放射能が高く，ニツスル小体あるいはリボゾームに対応する蛋白が代謝回転が速いことになるようです。また別の研究方法，例えばFolch-Pi のやり方で脳組織を分画してしらべることもできます。proteolipid 分画とresidual protein分画とでは代謝回転が非常にことなっており，蛋白の代謝回転は殆どすべてresidual protein 分画で起っています。一方，proteolipid 分画についてもP^{32}の代謝回転はおそいのですが，ペプチド分画のフオスフアチドは速い代謝回転を示しています。即ち，1つの蛋白分画についても，そのある部分（constituent）は他の部分とことなった代謝回転速度を示すことも考えられるわけです。つまり，脳にはマイオシンのような特殊な蛋白質はないのだと思われます。

次に，このような蛋白質の代謝回転と生理活動との関係はどうでしょうか。私どもの実験では，ある関係があることはわかりましたが，そうはっきりしたものではないようでした。ペントバルビタールや体温低下によって代謝回転は下りますが，電気ショックでは昂進は認められません。むしろ低下するぐらいでした。一方，Hydenらの実験で幼若なウサギの一群のlitter-mateを別にして，一方は完全に暗いところで，もう一方は明いところで育てると，網膜の神経節細胞のリボ核蛋白および全蛋白の量に著しいちがいができることが示されました。これは蛋白代謝と神経細胞の生理活動とが密接に関連していることを示すものです。神経細胞が正常の蛋白合成を行うためには刺激が必要なのでしょう。

さて次に，蛋白質代謝とブドウ糖代謝の関連について述べようと思います。in vivoでC^{14}グルコースを与えてそれがどのように代謝されるかをみるのが，最も手取り早

い方法です。ラットで実験してみますと，注射后数分で脳の遊離アミノ酸に大量にC^{14}が見出されますが，まだ蛋白，核酸，脂質などには殆ど入って行っていません。このことは，Geigerの灌流実験でも，また脳切片を用いたin vitroの実験でも示されたことで，脳髄に特異的であり他の臓器では1/10以下しかアミノ酸に入って行きません。アミノ酸のうちでは，C^{14}の80%もがジカルボン酸（グルタミン酸およびアスパラギン酸）に見出され，塩基性および中性のアミノ酸にはあまり見出されません。脳の蛋白質についても，そのグルタミン酸およびアスパラギン酸に大部分のC^{14}が見出されました。このようにグルコースからC^{14}が活発にグルタミン酸に入るのですが，それはグルコース代謝のどのような特徴にもとづくものでしょうか。

グルコースは脳組織でもクレブス回路によって酸化されるのですから，α-ケトグルタル酸とグルタミン酸の関係が脳組織では特別なのでしょう。この反応にはアミノ基転移反応も関係していると思います。アミノ基転移酵素は勿論脳組織で活発ですが，また肝臓などでも同様に高い活性を示しています。従ってこのことから，脳の特異性を説明することはできません。Tower らの脳ミトコンドリアを用いた実験によると，ピルビン酸，グルタミン酸，GABAさらにサクシニックセミアルデヒドはすべて高いＰＯ比を示すと言れます。従って彼の議論によると，所謂GABA回路が脳組織で活発で之れによってグルコースからのアミノ酸の形成が説明されると言れています。しかし，我々の実験では，GABAはピルビン酸の1/10以下の速度で酸化されるにすぎませんから，Towerらの言うようにGABA回路が主道であると信ずることはできないと思います。

これからのべる脳のミトコンドリアの実験は最近私どもの研究室でなされたものです。脳のミトコンドリアは肝臓のそれと大変ことなっており，ピルビン酸を基質とした場合，10倍も多量のα-ケトグルタル酸を蓄積します。即ち，クレブス回路の酵素系が特異であるために，脳のミトコンドリアはピルビン酸を好んで酸化し，α-ケトグルタル酸を蓄積するのであるようです。ピルビン酸とα-ケトグルタル酸とを同じ濃度で加えておくと，脳のミトコンドリアはピルビン酸を主に酸化し，肝臓のそれはα-ケトグルタル酸を主に酸化することが見られました。この場合には，2つの基質のあいだでお互に酸化を拮抗しているのだと思います。勿論，in vivoではα-ケトグルタル酸の蓄積はみられませんが，これはグルタミン酸の直接の前駆物質であり，脳にはグルタミン酸が蓄積すると言うわけでしょう。

このような脳のミトコンドリアの特異性はあるいはその基質に対する透過性の問題に基づくのかもしれません。しかし，私どものえた成績ではそれはやはりクレブス回路の酵素系の配列(organization)の相異にもとづくものと理解されます。

ネコを用いたin vivoの実験で以上の事情をはっきりとたしかめることができると思います。C^{14}グルコースを注射して30分后にしらべてみますと，血液中ではC^{14}は90%以上まだグルコースとして存在しており，肝臓などでもやはり大部分まだグルコースとして存在していますが，脳では僅か3%がグルコースとして存在するにすぎず，実に71%はアミノ酸のうちに見出されます。

以上のように，種々の実験方法による成績はすべて，脳のグルコース代謝系が特異であることを示しており，グルタミン酸に至る道が大きな代謝経路であることが明らかであると思います。

それでは，このような代謝系の特異性は脳の機能活動とどのような関係があるのでしょうか。有名なMullin の実験によれば，カエルの神経では刺激されたときにはグルコースの酸化はむしろ低下し，かわりにグルタミン酸が酸化されると言うことです。即ち，興奮のときにはグルタミン酸を直接のエネルギー基質として優先的に用いていることを示すものでしょう。もう1つはアンモニアの形成と神経活動の関連です。神経の興奮によってアンモニア形成が増加することは古く日本人田代によって発見されました。脳内アンモニアも興奮に伴って増加し，麻酔など脳活動の低下したときには減少することは確かな事実となっています。脳のアンモニアの濃度は多くの反応のバランスによってきまるものですが，それがアミノ酸の代謝と関連していることは確実です。この国の塚田によって生理活動とアンモニアの興味ある問題が研究されていますから，すでにご承知のことと思います。

蛋白質を分解するproteinaseも脳組織で非常に活性です。特に白質で活発であって，蛋白合成が神経細胞で活発であることと対照をなしていることは興味あることだと思います。

今日は，主に基礎的なお話しだけをしましたが，脳のアミノ酸代謝の問題は臨床的な面にも深く関連したものであり，私どもはその方向にも研究を進めていることを述べておわりにいたします。

——紹　介——

中枢神経の薬理学 1961年（Ⅱ）

前号につづいてBaker W. W. による1961年中の精神薬理学の論文表題を掲載する。目次（Contents）のうち，右半分の5．から9．（最後）までである。

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——ニュース——

WFNのシンポジウム

1962年6月, World Federation of Neurology, Commission of Neurochemistryの主催のもとにGothenburgで開かれたシンポジウムにつづいて, 1965年に英国で次のシンポジウムが計画されている。

"Variation in the chemical composition of the nervous system as determined by genetic and developmental factors"

やはり同じ年に(1965年)英国でVlth International Neurochemical Symposiumが予定されているが, その主題はまだ決定していない。

"行動の神経機構" シンポジウム

学術会議脳研連主催で6月1日(土), 東大医学部中央館で開かれた。

午前の部

(1)錐体路系と錐体外路系の解剖学的側面 (東大脳研 草間敏夫) : 指定討論者, 小島徳造(日大), 白木博次(東大)

(2)錐体路系と錐体外路系の体性感覚統禦(東大脳研 島津浩) : 指定討論者, 岩間吉也(阪大)

(3)視床下部刺激による学習行動と脳の刺激および脳の破壊(徳大精神 中尾弘之) : 指定討論者, 時実利彦(東大)

午后の部

(4)脳の組織化学(光顕的及電顕的)(阪大解剖 清水信夫) : 指定討論者, 吉川政己(東大)

(5)行動変化と脳内アミノ酸代謝 (東邦大生理 塚田裕三) : 指定討論者, 黒川正則(東大)

(6)行動系列の異常とその構成(群大精神 台弘)群大生理 平尾武久) : 指定討論者, 佐野勇(阪大神経) 八木晃(東大心理)

(7)動物実験による中枢神経作用薬物の解析—とくに脳波と行動の対応と分離の立場から— (塩野義研 山本研一) : 指定討論者, 小林龍男(千大薬理)

このシンポジウムの記録は"脳と神経"に掲載される予定になっている。

——書 架——

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編集委員（ＡＢＣ順）

鳩谷　竜　　川北　幸男　　高坂　睦年　　黒川　正則
成瀬　浩　　佐野　勇　　佐藤　倚男　　高垣玄吉郎
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昭和38年6月30日	印刷	神経化学　第2巻　第3号
昭和38年7月1日	発行	
編集者		(代表) 塚田　裕三
編集所	東京都大田区大森4丁目 東邦大学医学部第二生理学教室内	神経化学懇話会
印刷及製本	東京都文京区小石川町1丁目1番地	中央商会
表紙印刷所	東京都北区西ケ原3丁目46番地	杏林舎
発行所	東京都文京区曙町11番地	緒方書店

会員外の方で本誌の希望者は，実費でお頒けしますから上記の編集所宛にお申出下さい

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