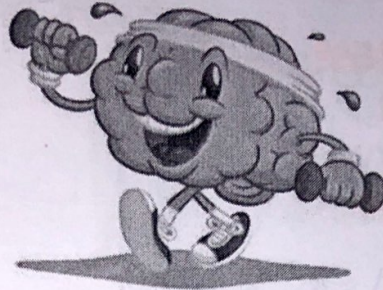




Brain Energy Metabolism I



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Central Nervous System



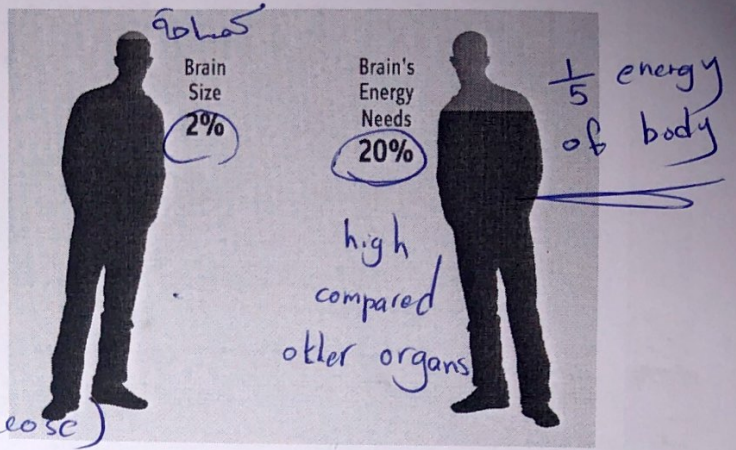
- Nervous system is that part of our body which coordinates all **voluntary and involuntary missions** and transmits signals to and from various parts of the body
- Nervous system is divided into two main parts: central nervous system (CNS) and peripheral nervous system (PNS)
- The **CNS** consists of *Brain* and *Spinal cord* whereas **PNS** is composed mainly of *Nerves* that connect the CNS to every other part of the body
- The *brain* is an information **processing** center like *وحدة معالجة مركزية* computer. To function properly, cerebral tissue requires constant supply of energy

حتى لا يتخلف

Brain Energy Needs



- Although the human brain constitutes only **2%** of the total body weight, its **metabolic demands are extremely high**
- The brain receives **15%** of the cardiac output, **20%** of total body oxygen consumption and **25%** of total body glucose utilization (circulating glucose)



- The brain needs a constant supply of oxygen and glucose to function. Cerebral **hypoxia** can lead to **irreversible neuronal damage** after about 5 minutes. also, **severe hypoglycemia kills the neurons.** (لأنها خلايا لا تتجدد)

من طرفه
من طرفه

who the emergency? Brain ← # the most vulnerable organ to shortage O₂ + glucose?
by po or hyperglycemia?

Brain Energy Expenditure



- **Glucose** is the primary energy substrate of the brain, where it is almost entirely oxidized to **6CO₂** and **6H₂O** through its sequential processing by **glycolysis**, **tricarboxylic acid (TCA) cycle** and the associated **oxidative phosphorylation** resulting in **30 ATP molecules/ glucose** (الوحيد) (حرق كالم → 32 in heart)
- **Na⁺/K⁺-ATPase pump**: is an **ATP-dependent transporter** found in the membrane of neuronal and glial cells responsible for the active transport of **3 Na⁺ out** and **2 K⁺ in** (active) against **Con gradient**
- The main energy-consuming process in brain is the maintenance of ionic gradients across the plasma membrane which is achieved by ionic pumps fueled by ATP, particularly **Na⁺/K⁺-ATPase pump**

بعض الموضوع
كله حركة
أحداث
maintenance
their original
value
(pumps)

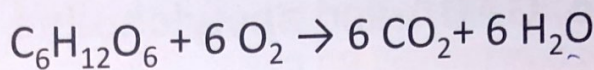
- وظائف خلايا الدماغ
- 3 ① generation AP by axons
- ② release neurotransmitter
- ③ generation AP post synaptic
- ④ glial cell reuptake neurotransmitter
Astrocyte reuptake glutamate

→ volume of CO₂ eliminated to volume of O₂ consumed

Oxygen-Glucose Uncoupling



- The **respiratory quotient** of brain (**RQ**) is very close to 1. This means that the brain metabolism utilizes almost exclusively carbohydrate sources, particularly glucose



in Brain
الدماغ لا يعزى
إلا إلى القلوكوز

$$\text{Respiratory Quotient} = \frac{vCO_2}{vO_2} = \frac{6CO_2}{6O_2}$$

$$RQ = 1$$

→ Brain

range

$$0.7 - 1$$

0.7 → fat

0.8 → proteins

1 → Carbohydrates mainly glucose

Oxygen-Glucose Uncoupling



- O₂ consumption rate of brain is 160 mmol / 100 g/min but the measured glucose utilization rate is 31 mmol / 100 g/min which is slightly higher than the **predicated value** of 26.6 mmol / 100 g/min

العجز

expected or calculated value (متوقعة)

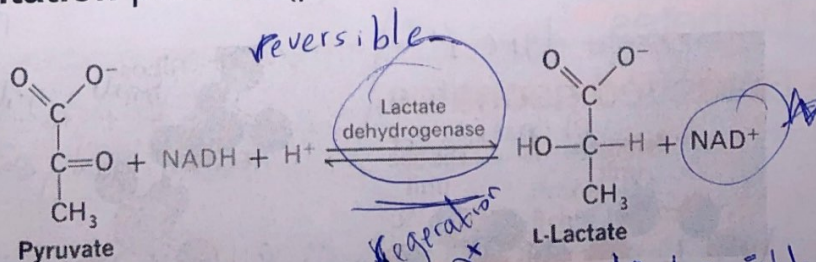
- The fate of the excess 4.4 mmol of glucose:

ما الذي سلافة بال

الفرق بين القمتين

- Stored as **glycogen** in astrocytes
- Limited amount of glucose is metabolized only by glycolysis where the pyruvate is converted to lactate via **anaerobic fermentation** process (particularly in astrocytes)

استهلاك آخر



↳ has بوابة in glial cells + neuronal cells

* من كل الجلوكوز الذي يتصلب للدماغ يتم حرقه

Oxygen-Glucose Uncoupling



3. Essential constituent of **glycolipids** and **glycoproteins** present in neural cells
4. Utilized in the synthesis of brain neurotransmitters: **glutamate, GABA** and **acetylcholine**

• There is **uncoupling between O₂ consumption and glucose utilization in cerebral tissue**

- This indicates that metabolic needs of brain tissue are partially met by non-oxidative metabolism of glucose
- Different active areas in brain tissue are associated with high level of **lactate**

* كل ما بقي سوية جلوكوز تأخذ جزءا كبيرا من neurons تخزنها على شكل glycogen وكل ما يحتاج تكبره وتغطي على شكل Lactate

Energy Substrates for Brain



Adaptive mechanism (Ketone bodies) (تستخدم الجلوكوز (Ketone))

1. Glucose is the **exclusive substrate for oxidative metabolism** used to produce energy in the form of ATP molecules under aerobic conditions and very limited extent under anaerobic conditions (fermentation) **Lactate** in astrocyte
1. Ketone bodies particularly **acetoacetate (AcAc)** and **D-3-hydroxybutyrate (3-HB)** become energy substrates for the brain in particular circumstances:

- Ketogenic condition
- **Starvation**
 - **Diabetes type 1**
 - **Breastfed neonates** (not pathologic)

يعرف Bab

3) acetone يطلع مع التنفس - يكون دائما في رية في الدم

1+2) # بروحها للدم والدماغ ويبنى يخدمهم ليكون طاقة

الدماغ لا يمر ال Pat لكنه يدخل **in directly** على شكل Ketone

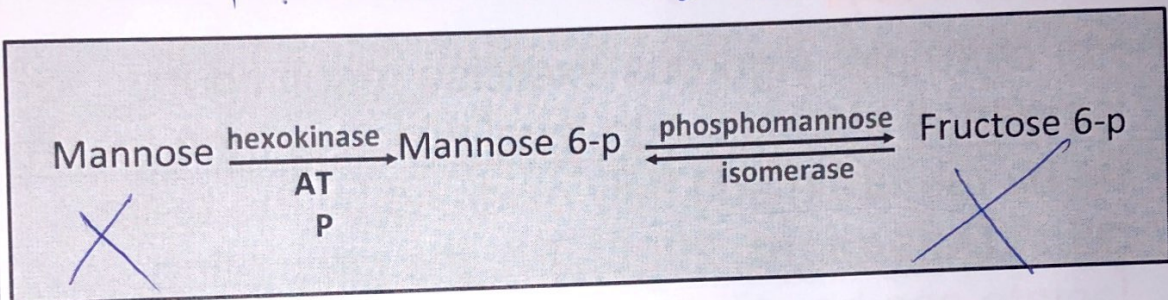
Energy Substrates for Brain



3. Other substrates like mannose, pyruvate and lactate have been tested as alternative substrates to glucose for brain energy metabolism:

- **Mannose:** it can cross BBB readily but is **not normally present in the blood** so it has **no physiological significance**

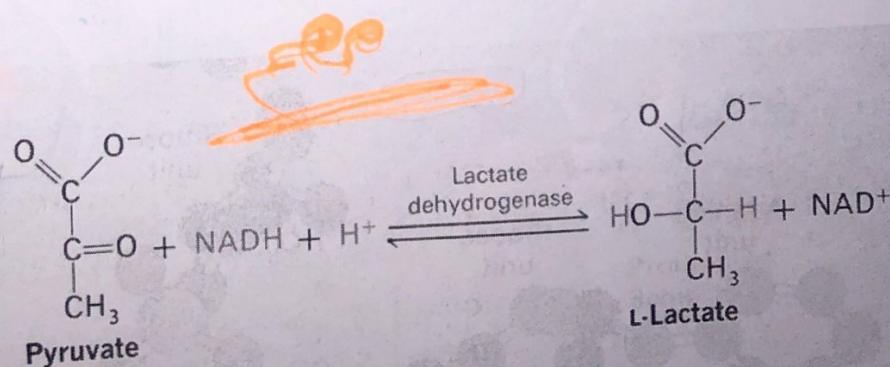
عملوا تجارب
يتم للدماغ لكنه اصلاً لا يتواجد بالدم



Energy Substrates for Brain



- **Pyruvate and lactate:** when these **monocarboxylate molecules** are formed within cerebral tissues from the glucose that has been crossed the BBB, pyruvate and lactate in fact become the **preferential energy** substrates for activated neurons.



Energy Substrates for Brain



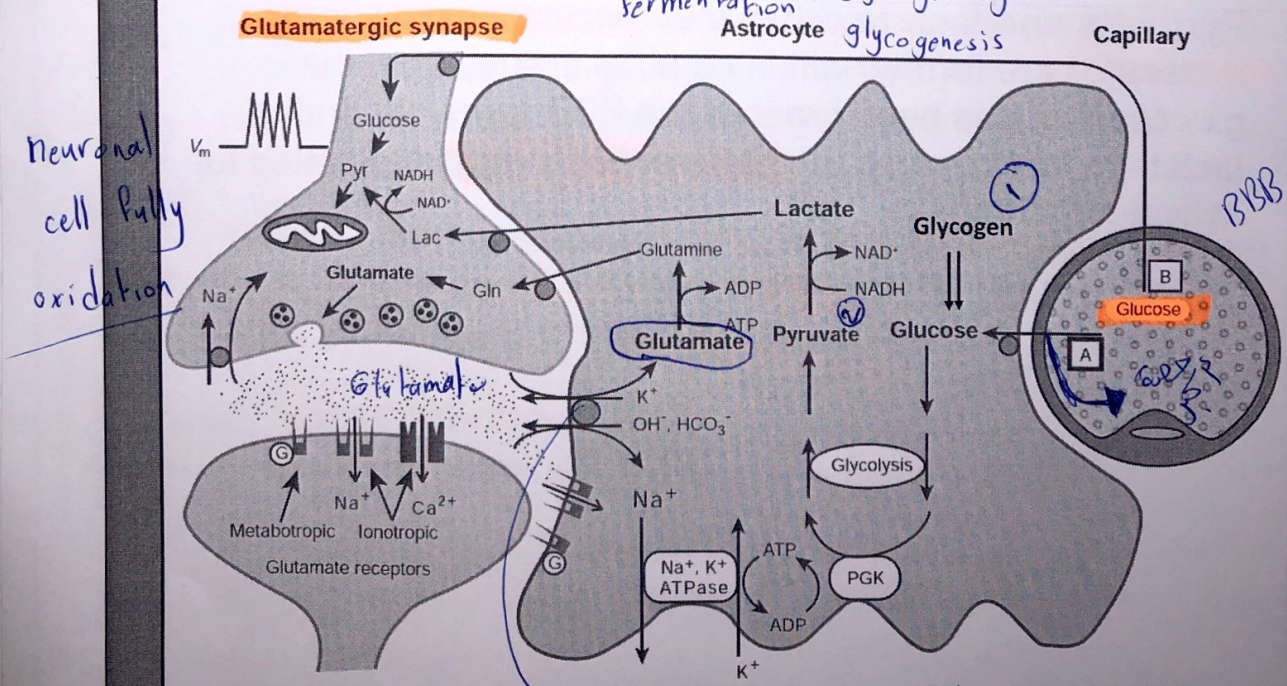
- Until recently, circulating pyruvate and lactate was thought that they have limited permeability across BBB thus circulating pyruvate and lactate can't serve as substrates for brain energy metabolism (**several contradictory studies ???**)
- For example, vigorous exercise resulting in increased blood lactate level which is then taken up by the brain and fully oxidized by the brain cells (**Dalsgaard, 2006**). So, the circulating lactate can be utilized as energy substrate for human brain

منه يسا الموجود بالدماع فقط
 اله بوابان حكي
 في الدماغ

Cell-Specific Glucose Uptake and Metabolism



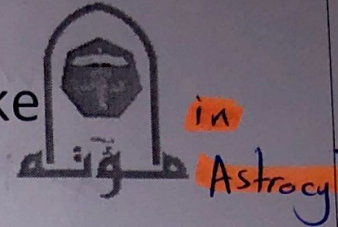
pyruvate + gly cogenlysis
 fermentation + glycogen synthesis
 Astrocyte glycogenesis



reuptake glutamate by astrocybe with Na

Glycolysis is mediated by Glutamate Reuptake

associated with induction of glycolysis



- The basal rate of glucose utilization is high in astrocytes than in neurons
- In astrocytes, glucose utilization is mediated by glutamate reuptake via specific transporters
- Glutamate is co-transported with Na^+ ions which increases intracellular Na^+ concentration
- This activates Na^+/K^+ ATPase pump and consequently induces glycolysis
- Hence, neuronal activity is coupled with glucose utilization in brain
- Indeed, during activation there is an increase in lactate release by astrocytes to be utilized by neurons

الجلوكوكو جن في الدماغ، العضلات ليس *generus* مثل الالكيد التي يبعثه
لباني الجسم، الدماغ، العضلات تحتفظ فيه مشان نفعها فهي كيف تمنع خروج

~~phosphatation~~

الترنم *glucose 6-phosphatase* هو المسؤول عن ازالة P ليضع بخروج
glycogen وهو من موجود في الدماغ و العضلات

كيفية *astrocyte* تحمي ال *glycogen* لل *neuronal cells*
تحولة الى *Lactate* عنان يطلع من البرابات

يحقق على الخلايا العصبية
خلايا كثيرة
رغم انه ATP 28
preferred substrate