The effect of Thai herbal medicine on learning & memory mechanisms, and vascular dementia

Introduction

Brain functions

- Sensation, movement, language, thought, and etc.
- Learning
  - A process: new information is acquired
- Memory
  - A process: the previously acquired knowledge is stored and maintained for later use
- Behaviors
  - The response of an individual, group, or species to its environment
  - Affected by Learning and memory
  - Normal vs Abnormal behaviors

Learning and Memory

- Human brain
  - A network of more than 100 billion individual neurons
  - Neurons are interconnected in systems
  - Neural circuits
- Hippocampus
  - Medial temporal lobe
- Long-term potentiation
  - A putative neural mechanism
  - Associative memory formation and storage in mammalian brains

Dementia

- Impair functions of multiple brain systems
- Learning & memory and cognitive dysfunctions
- Interfere with daily activities & the quality of life

Types of dementia

- Alzheimer’s disease: 54%
- Vascular dementia: 26%
- Other: 20%

Vascular dementia (VaD)

- Blockage of cerebral blood vessels
  - Chronic cerebral hypoperfusion
- Progressive decline in cognition
  - Cognitive & memory impairments
- Neuronal death and white matter damage

Pathophysiology of Chronic cerebral hypoperfusion

- Oxidative stress
- Neurovascular pathology
  - Microvascular basement membrane thickening
  - Collagen deposition
- Neuronal damage
  - Apoptosis
- Glial activation (astrocyte and microglia)
  - Pro-inflammatory cytokines and chemokines
- Inflammation (Doyle et al., 2008)

Learning and memory impairment
**Bacopa monniera (BM); Brahmi**

- A Thai herbal medicine
- Asian countries such as Nepal, India and Thailand
- Learning & memory, intelligence enhancer, antiepileptic activity
- Active ingredient: saponin glycosides
  - Non-polar glycosides (Pajau et al., 2011; Abascal et al., 2011)
  - Cross the blood brain barrier (BBB) (Pardridge WM., 1999)

**Introduction**

Thorne Research, 2004; Boonyaprapath et al., 1999; Kumar et al., 2006; Alternative Medicine Review, 2004

**Effects of BM extract on learning & memory**

- Antioxidant
- AChE inhibitor
- Anti-inflammation
- Learning & memory enhancer

**Protective effect against Chronic cerebral hypoperfusion**

- Drug administration:
  - H2O
  - BM 120 mg/kg of BW
  - BM 160 mg/kg of BW
  - BM 240 mg/kg of BW

- Histological study:
  - Cresyl violet staining
  - Mean total number of survival neurons in CA1, CA3 & DG

- Transcardial perfusion

- Behavioral study:
  - Morris water maze (MWM) task
  - Camera → Visual cues
  - 12cm Hidden platform
  - 50 cm Visual cues

- Acute hippocampal recording:
  - Long-term potentiation
  - Mean escape latencies
  - Mean retention times

- Material and methods:
  - 2 step 2-VO model
  - Chronic cerebral hypoperfusion

- Behavioral study:
  - Morris water maze (MWM) task

- Material and methods:
  - Visible trial
  - Acquisition trial
  - Probe trial

- Days

**Behaviors & methods**

- Visible trial
- Acquisition trial
- Probe trial

**Result**

- Effects of BM extract on Spatial learning & memory

- 2-VO: 2-vessel occlusion
- MWM = Morris water maze

- Days

- Visible trial
- Acquisition trial
- Probe trial
The mean total numbers of surviving hippocampal neurons

Material and methods

CA1
CA3
DG

345 x 300 µm²/crop or 0.1 mm²

Total area = 0.3 mm²

Effects of BM extract on surviving neurons in CA1 subregion

Result

| Sham | 2-VO | 2-VO + BM 120 mg/kg | 2-VO + BM 160 mg/kg | 2-VO + BM 240 mg/kg |

Result

Effects of BM extract on the mean total number of surviving hippocampal neurons

Material and methods

Result

| Sham | 2-VO | 2-VO + BM 120 mg/kg | 2-VO + BM 160 mg/kg | 2-VO + BM 240 mg/kg |

Result

Effects of BM extract on Long-term potentiation

Material and methods

<table>
<thead>
<tr>
<th>Acute hippocampal recording</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stimulation</td>
</tr>
<tr>
<td>Schaffer collateral fibers</td>
</tr>
<tr>
<td>Record</td>
</tr>
<tr>
<td>Dendritic layer of CA1 area</td>
</tr>
<tr>
<td>Excitatory postsynaptic potential (EPSP)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Long-term potentiation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Long-term enhancement of postsynaptic response</td>
</tr>
</tbody>
</table>

Conclusion

| Brahmi extract demonstrated neuroprotective effect against chronic cerebral hypoperfusion |
| Prevent the learning and memory impairment |
| Reduce of hippocampal cell death |
| May be mediated by anti-inflammatory and anti-oxidative activities |

| Memory enhancing effect of the extract to exhibit its activity in hippocampal synapses |
| Enhance of LTP magnitudes |
| Maybe mediated by anti-acetylcholinesterase activity |
Ongoing projects

- The effect of Brahmi extract on molecular cascades in chronic cerebral hypoperfusion
  - Molecular techniques
- The role of sodium leak channel, non-selective (NALCN) in learning and memory
  - Induction of siRNA into neurons via viral vectors
  - Blockage of NALCN gene expression

Acknowledgement

- Assoc. Prof. Kanokwan Tilokskulchai
- Dr. Sompol Tapechum
- Mr. Sarayut Vattananupon
- Ms. Charkriya Promsuban
  - Physiology Department, Siriraj Hospital, Mahidol University
- Assist. Prof. Tawee Laohapand
- Assoc. Prof. Pravit Akarasereenont
  - Center of Applied Thai Traditional Medicine, Siriraj Hospital
- Dr. Arnaud Monteil
  - Institute of Functional Genomics, France