

Non-pharmacological treatments of depression: neurogenesis & neuroplasticity

(exist in space + change over time)

CANMET guidelines, 2016

Dr. Arif Syed Oct. 22, 2017

Physical treatments for mild to moderate depression:

- 1) **Exercise**: (level I evidence + severe) at least 30 min, 3 x/week x 9 wks (=27 sessions)
- 2) **Light therapy**: (level I evidence) 10,000 lux intensity for 30 min/day in AM x 6wks
- 2) **Yoga**: (level II evidence) average of 3 sessions/wk for 2-3 months (=26 sessions)
- 3) **Acupuncture** (level II evidence) daily to weekly for 20-30 min average =20 sessions
- 4) **Sleep deprivation** (level II evidence + severe) 40h awake + 8h sleep/ 3-4h sleep a day

Natural health products for mild to moderate depression:

- 1) **St. John's wort**: (Level I evidence + severe) use 300mg tid, on average for 2-3 months
- 2) **Omega-3**: (Level I evidence + severe) use EPA+DHA 3-9g/day, average for 2-3 months
- 3) **SAME**: (Level I evidence + severe) use 400 mg tid, on average for 2-3 months
- 4) **Acetyl-L-carnitine** (L II), **saffron** (L II), **DHEA** (L II), **folic acid** (L II-adj), **lavender** (L III-adj). Negative results for Inositol, Tryptophan, Rhodiola (roseroot)

Many of the above interventions overlap with what is known below to make a protein called **BDNF**

Medical interventions: antidepressants, light Tx, ECT, deep brain stimulation, TMS

Hormones: melatonin, thyroid hormone, testosterone, progesterone, 17b-estradiol,

Foods and supplements: omega-3, folic acid, blueberries, curcumin/turmeric, ginseng, cacao (70% dark chocolate), Zinc, vitamin D, quercetin, resveratrol

Neurostimulating Activities: exercise

acupuncture

sleep deprivation

intellectual stimulation

meditation / reflection

touch / sexual intimacy

socialization

enriched environment / housing

NEUROGENESIS

The NEW production of neuron stem cells via BDNF- brain derived neurotrophic factor
More quickly in young brains, but still slowly present in depressed/aging brains until we die.
Eg- song birds sing new songs every year!

Neurogenesis *actively* occurs in the olfactory bulb and hippocampus (esp. 4 wks = 28 d after ADs)
but *dormant* in: septum-emotion, striatum-movement, and spinal cord.
In other places, once brain cells are lost, they cannot be replaced

There are two ways to increase the number of neurons (100 billion) in the brain:

- 1) The new production of neurons: neurogenesis-generally by BDNF
- 2) Extending the life of neurons: neuroplasticity-generally by neurostimulation/learning

A synergistic relationship between: **Neuroplasticity ↔ Neurogenesis**

Neuroplastic activities lead to neurogenesis brain cell growth (first page)
found in neurostimulation activities causing anticipatory growth adaptation by BDNF production

However, *Neurogenesis also leads to Neuroplasticity*
found in BDNF growing connections of neurons in the **critical period** of brain development.
Eg- kitten's brain must receive visual stimulation from 3rd-8th week, if not, its blind for life!
Eg- goslings critical period to bond is 15 h-3 days, if only exposed to a human, it wouldn't go to mother
Eg- children's language development ends at 8-13 years old, harder to learn second language after this

Plasticity is when sets of neurons connect together: "neurons that fire together, wire together"

NEUROPLASTICITY

Definition: Neuroplasticity is the ability of the brain to change, or mold, for better or for worse, throughout the individual's life span.

"Neurons that fire together, wire together"

Connections between brain cells are based on stimuli from learning, activities, or the environment

Synaptic changes- (days to weeks) increased synapse connections and receptors, better signal
Neuron changes- (after 28 days) production of new protein (BDNF) and dendrite branching
Circuit changes- (6 months-2 years) cortical remapping of new networks of brain functions

Positive changes: better memory and thinking, new skills, faster mental speed and control.

Negative changes: pain amplification, decline in performance with non-use or injury

Stages of Neuroplastic healing:

- 1) Neurostimulation- overcome dampening of dormant cells by putting in energy through:
 - a. light sunshine, light therapy
 - b. sound music, spiritual recitals and affirmations
 - c. electricity acupuncture, TENS, ECT
 - d. vibration massage, deep brain stimulation
 - e. movement exercise: walking, yoga, tai chi, sports, etc.
 - f. thoughts knowledge, reflection, meditation, visualization

- 2) Neuromodulation-restoring internal balance (via interneurons) by resetting overall level of arousal (RAS-reticular activating system), and timing of systems of automatic/autonomic sympathetic (fight or flight, or freeze response) + parasympathetic (rest-digest-repair, relaxation response)

- 3) Neurorelaxation- catching up on lost sleep, and storing energy for the efforts of recovery

- 4) Neurodifferentiation & learning- now that dormant cells are active, brain and bodily functions are awake, stabilized, and rested, now you are ready to pay attention and to learn!

Some qualities of neuroplasticity

A. Competitiveness: “if you fail to plan, you plan to fail”

Repeating good behaviours / knowledge in childhood sets the first automatic patterns: protective Size and space of brain map is turned over to the skills/learning we are actually currently using. Bad habits if repeated regularly, take over the brain map from good activities: hard to unlearn
Solution: Doing good deeds continuously, even if small (preserves your brain map)

B. Learned Non-Use: “Use it or loose it”
“Be avid for what benefits you, and do not consider yourself incapable”

If you stop trying, brain maps and circuitry deteriorate, then you really will be incapable
In older adults, atrophy of brains attentional system (nucleus basalis) results in lack a strong signal enough to register or remember daily information.
Solution: to learn something NEW with intense FOCUS ‘from the cradle to the grave’
Eg- brain exercise games, challenging puzzles, career change with new skill set, new language

C. Noisy Brain: “muddy in, muddy out”

(Internal) Damaged/dormant neurons fire irregularly causing abnormal signals=background noise

(External) White noise, continuous stimulation during critical period leads to excessive BDNF release and undifferentiated over-connectivity and overexcitability to any stimuli after this period

Eg- closer children lived to an airport, or to noisy highway, the lower intelligence they had

Solution: reduce noise with **periods of non-stimulation** (boredom/meditation)

Solution: strengthen useful signals through Neuroplastic brain exercises: **small changes done slowly and repetitively (with reward/reinforcement) AND maximal focused awareness**

Optimize signal/noise ratio in brain circuits results in sharper observations & stronger memory

One of the most well studied forms of Neuroplastic exercise combines:

intellectual stimulation (new knowledge) + focus + socialization + reflection ... Psychotherapy.

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Psychological treatments for major depression:

ACUTE: level I evidence for CBT, IPT-interpersonal, BA-behavioural activation

MAINTAINANCE: level I evidence for CBT and MBCT-mindfulness based cognitive

Lower levels of evidence for: problem-solving therapy, short term psychodynamic, telephone and internet delivered CBT, acceptance & commitment therapy, motivational interviewing

Acute CBT more effective in preventing long term relapse than brief AD-antidepressant use

For long-term, no difference relapse risk for 1-2 years between compliant use of ADs vs CBT

Starting CBT after stopping full course of AD treatment, prevented relapse by 20% cf no CBT

Most efficacious length of therapy? NO difference in *number* of session overall, but there was a strong positive association for increased *frequency* per week (better Neuroplastic training?)

Most efficacious parts of therapy?

Therapeutic alliance: emotional bond / goal consensus / mutual co-operation

Therapist's qualities: empathy / collecting patient feedback / positive regard

Most efficacious results?

For moderate-severe MDE, **combining** AD meds + CBT were more effective than either alone

BDNF producers + neurostimulation work

NEUROGENESIS + NEUROPLASTICITY