European Psychiatry 30 (2015) 75–81

Contents lists available at ScienceDirect

European Psychiatry

journal homepage: http://www.europsy-journal.com

Review

Developing cognitive-emotional training exercises as interventions for mood and anxiety disorders

B.M. Iacoviello *, D.S. Charney

Department of Psychiatry, Icahn School of Medicine, Mount Sinai, NY, USA

ARTICLE INFO

Article history:
Received 25 September 2014
Received in revised form 29 September 2014
Accepted 29 September 2014
Available online 28 October 2014

Keywords:
Cognitive
Emotional
Training
Plasticity
Intervention

ABSTRACT

There is an urgent need for more effective treatments for mood and anxiety disorders. As our understanding of the cognitive and affective neuroscience underlying psychiatric disorders expands, so do opportunities to develop novel interventions that capitalize on the capacity for brain plasticity. Cognitive training is one such strategy. This paper provides the background and rationale for developing cognitive-emotional training exercises as an intervention strategy, and proposes guidelines for the development and evaluation of cognitive training interventions with a specific focus on major depressive disorder as an example.

There is an urgent need for more effective treatments for mood and anxiety disorders. Major depressive disorder (MDD) is a particularly disabling mood disorder associated with significant morbidity, mortality and public health costs [37,79]. Despite the development of numerous pharmacotherapy and psychotherapy options for the treatment for MDD, roughly 30–40% of patients fail to achieve adequate therapeutic response to currently available treatments [65,74]. To address this need for novel treatments, a Concept Clearance was issued as part of the NIMH Strategic Plan in 2011 [51] for "research that translates emerging findings on the neuroscience and behavioral science of mental disorders into novel psychosocial (e.g., cognitive strategies and innovative behavioral approaches) and other non-pharmacological interventions... that will alter dysfunctional neural circuits and psychological processes underlying mental disorders to reduce symptoms". Fortunately, as our understanding of the intersection between neuroscience, cognitive science and psychiatry grows, so do opportunities for the development of innovative translational intervention strategies. In this paper, we describe the rationale and method for developing cognitive-emotional training interventions for mood and anxiety disorders, and provide an example for MDD.

1. Harnessing brain plasticity

Plasticity refers to the brain's ability to change as a result of experience, and modify future responses to the same and related stimuli [60]. Plasticity can involve functional or structural changes: strengthening or weakening of connections between neurons, formation of new synapses or loss of existing ones [6,10], or in unusual circumstances altered birth and growth of new neurons.

A fundamental component of how brain plasticity occurs is the synapse between nerve cells. Synaptogenesis and synaptic pruning refer to the idea that individual connections within the brain are constantly being removed or recreated, largely dependent upon how they are used [6,10]. If two nearby neurons often produce an impulse simultaneously, their cortical maps become integrated via the growth of new synapses or strengthening existing ones. Conversely, neurons that do not regularly produce simultaneous impulses form different maps and the synaptic connections between them weaken. Thus, with experience, the number and strength of synapses in the brain can change over time, influencing neural network functioning. Change in the intrinsic excitability of neurons, termed whole cell plasticity or homeostatic plasticity, is also an important contributor to brain plasticity [39]. Changes to ion channel function in the axon, dendrites, and cell body result in changes in the integration of excitatory postsynaptic potentials (EPSPs) and inhibitory postsynaptic potentials (IPSPs). Modification of the electrical properties of neurons can affect synaptic

* Corresponding author. One Gustave L Levy Pl, Box 1230, New York, NY 10029, USA. Tel.: +21 2 241 6383; fax: +21 2241 3354.
E-mail address: brian.iacoviello@mssm.edu (B.M. Iacoviello).

http://dx.doi.org/10.1016/j.eurpsy.2014.09.415
0924-9338/

integration, subthreshold propagation, spike generation, and other fundamental mechanisms of neurons at the cellular level. These individual neuronal alterations can result in changes in higher brain function, especially learning and memory.

The growth of new neurons, also termed neurogenesis, may also play a part in brain plasticity, although the contribution of neurogenesis to brain plasticity is likely smaller compared to synaptic changes and homeostatic plasticity. Hippocampal neurogenesis has been demonstrated in non-human primates and humans [20,24], and the subventricular zone (SVZ) was identified as a site of neurogenesis and self-renewing neurons in the adult brain [47]. Along with the subgranular zone of dentate gyrus, the SVZ serves as a source of neural stem cells in the process of adult neurogenesis. Some have also suggested that adult neurogenesis occurs in regions within the brain not generally associated with neurogenesis including the neocortex [25,67,82]. Thus, evidence is emerging that neurogenesis occurs in the brain, with the strongest evidence for neurogenesis occurring in the dentate gyrus and subventricular zone. Together, synaptogenesis, synaptic pruning, homeostatic plasticity and, to a lesser degree neurogenesis begin to explain the mechanisms by which brain plasticity can occur on structural and functional levels.

Studies suggest that cognitive interventions can influence brain plasticity. In a neonatal ventral hippocampal lesion rat model of schizophrenia, cognitive training in adolescent rats protected against cognitive control impairments and altered hippocampal neural activity typically observed in adulthood [43]. Human PET and fMRI studies of cognitive therapy for depression and anxiety have identified functional changes in neural circuits involved in cognitive control and emotion regulation [15], and implicit cognitive priming for emotional stimuli demonstrated a persistent effect on subsequent amygdala response [62]. A systems neuroscience rationale for cognitive training interventions has been proposed, emphasizing the distributed nature of neural circuits that support cognitive and affective processing, as well as their plasticity [75]. During successful learning neural circuitry is altered, cognitive/affective inputs and action outputs are represented by larger and more coordinated populations of neurons that are distributed throughout multiple brain regions and across multiple levels of processing. Cognitive interventions could affect changes in brain neurobiology and function, and such changes are consistent with clinical effect.

2. Prior approaches to target maladaptive cognition

2.1. Cognitive approaches that explicitly target maladaptive cognitive processes

Explicitly addressing maladaptive cognition in the treatment of mood and anxiety disorders is not necessarily a novel intervention strategy. One example is cognitive therapy, where maladaptive core beliefs, cognitive distortions and automatic thought patterns are directly challenged and reformulated. Cognitive therapy has received much empirical support for its ability to alter cognition, affect brain changes, and improve symptoms [15]. Interpretation bias modification is another example in which patients are trained through repeated learning opportunities to make neutral or positive interpretations for ambiguous hypothetical events as opposed to the negative interpretations they would usually make [48]. Studies of healthy individuals suggest that interpretation biases can be modified to be more positive [48], and in clinical populations interpretation bias modification has been shown to significantly reduce negative interpretation biases, and this precedes mood improvement [5,30].

2.2. Cognitive approaches that implicitly target maladaptive cognitive processes

Cognitive theories of anxiety hold that early, automatic orienting of attention toward particular classes of stimuli (e.g., threat cues) plays a critical role in the etiology and maintenance of anxious mood. In Attention Bias Modification (ABM; [3]), patients are implicitly trained to attend away from negatively-valenced stimuli and toward a simultaneously presented neutral stimulus. Studies have demonstrated that change in attention bias can result in significant improvement in anxiety symptoms [28]. This is consistent with the observation that anxious individuals show increased vigilance for threat during free viewing and visual search, and show difficulty disengaging from threat in visual search tasks. In contrast, depressed individuals tend not to show the same vigilance for threat during free viewing, but are characterized by reduced orienting to and maintenance of gaze on positive stimuli and increased maintenance of gaze on dysphoric stimuli [1]. Still, studies using ABM procedures have shown results reducing MDD symptoms [78,80]. The results of ABM studies for mood and anxiety symptoms must be considered with caution when they do not report changes in underlying attention biases while reporting improvements in clinical symptoms, raising questions about the mechanism of effect. Some have demonstrated that the direction of ABM training may not be important. In one study of socially anxious patients, attention training toward threat or away from threat, compared to no training, was associated with attenuated anxiety during a social stress induction challenge [38]. Perhaps exercising and training cognitive control for emotional information processing is the key mechanism of effect in ABM regardless of the direction of training.

2.3. Cognitive control training and neurobehavioral therapies

Enhancing cognitive control has become a target for intervention in mood and anxiety disorders. Mindfulness training, in which patients are trained to bring awareness to their internal and external experiences in the present moment, is an example of attentional control training [73]. Mindfulness training has shown effects on cognitive processes, such as selective and executive attention [8] as well as clinical effects on mood, emotion regulation, decreased reactivity and increased flexibility of responses [2,12]. In 2007, Siegle et al. [71] reported that a metacognitive attention training exercise aimed at enhancing functioning of prefrontal cortical brain regions resulted in improvement in cognitive control and MDD symptoms. Others have since reported on the efficacy of this [7] and other similar cognitive or attentional training exercises [59] in dysphoric or depressed patients. These are examples of neurobehavioral therapies (NBT); therapies designed to target a known biological mechanism of the disorder using cognitive or behavioral techniques to affect change in that mechanism. Several lines of evidence provide support for the NBT concept:

- cognitive and behavioral psychotherapies employ an analogous approach, directly target mechanisms (core beliefs, etc.) that underlie maladaptive thought and behavior patterns;
- neurofeedback can effectively train patients to modulate their own neural activity, suggesting a cognitive exercise could affect change at the neurobiological or neural circuitry function level;
- cognitive rehabilitation has shown promise in identifying affected brain regions and functions using neuropsychological testing and neuroimaging, and using targeted, repetitive behavioral exercises to strengthen aspects of cognition, such as attention, memory, and cognitive organization which have