The effect of negative mood and major depressive episode on working memory and implicit learning

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Major depressive episode (MDE) is one of the most common psychiatric diagnoses and it has long-term mental and physiological consequences. The status of cognitive functions is of specific importance in case of affective disorders, due to their influence not only on patients' behaviour, but to a certain extent also on the success of psychotherapy. In addition, examining the impact of mood and affective disorders on cognitive functions also helps us understand the relationship between brain plasticity and neurocognitive networks. While the relationship between explicit, conscious memory and mood are relatively well-explored, the effect of mood and affective disorders on working memory and implicit sequence learning received less attention. The present review aims to overview available results in these less-explored areas. Research suggests that while working memory performance shows impairments in MDE and in some specific mood conditions, effects of affective disorders and mood on implicit sequence learning are more contradictory, highlighting the need for further studies in this field.
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Working memory (WM) and implicit, non-conscious learning (IL) play a crucial role in our everyday behaviour by supporting adaptation to the environment and decision-making processes. While WM helps process, maintain and manipulate information in the short term and plays an important role in cognitive and behavioural control, IL plays a key role in mapping the structures and sequences of the environment and supports automatic, intuitive and skills-related behaviour. The status of these cognitive functions is important not only in the case of healthy people, but also in the case of mood disorders, since these define the behaviour of the patients and the success of their therapy. In addition, examining how mood and mood disorders affect WM and IL also helps us understand the relationship between brain plasticity and neural networks. While the relationship between explicit, conscious memory and mood are relatively well explored, the role of mood on WM and IL received less attention. The present qualitative review aims to fill this gap.

Major depressive episode (MDE) is one of the most common psychiatric diagnoses and it has long-term mental and physiological consequences (Sartorius, 2003). This disorder is associated with psychological, behavioural and emotional symptoms which have been studied thoroughly, making it a well-explored medical field, while other symptoms, including somatic symptoms and some cognitive symptoms have not been examined so comprehensively and their anatomical-neurochemical backgrounds are not so clear yet (Rijavec and Grubic, 2012). As defined by DSM-V, the most common symptoms of MDE are constant bad mood, lower level of interest and the ability to be happy, enervation, problems with concentration, irritated mood, insomnia or hyper-

somnia, psychomotor agitation or retardation and the occurrence of suicidal thoughts (APA, 1995). It is important to note that the illness, in addition to its symptoms affecting the quality of life, can also lead to severe consequences for the patient, especially if not treated properly (Sartorius, 2003; Bair et al., 2003). More than 50% of the people with depression suffer a relapse in the two years following the first episode and 80% of them suffer more than one MDE during their lifetime (Mueller et al., 1999). For these reasons, it is extremely important not only to identify MDE early in its course and to identify the characteristics of not only the acute, but also the premorbid phase, but also to identify both trait and state-like alterations, and to identify markers which could distinguish between major depressive episodes associated with different types of affective illness. Better mapping and understanding of the neurocognitive characteristics typical of major depression could this way contribute to better screening and diagnosis of the disease.

The former belief that mood is set by specific neural networks (Mayberg et al., 1994), has been supported by the results of recent brain mapping methods, according to which the major symptoms of MDE are initiated by the abnormal change of the frontosubcortical circuitry, such as the lowered perfusion of the frontal, temporal and striatal areas (Tekin and Cummings, 2002).

MDE can evolve on a diverse etiological background in case of different types of affective disorder. Despite the diverse etiological path and psychiatric case history, MDE has strong pathophysiological and neuropsychological characteristics (Hammar and Ardal, 2009), some of which become emphasized as the symptoms worsen (Farrin et al., 2003), while others calm down during remission (Douglas and Porter, 2009).

One of the main symptoms of major depression is the alteration of cognitive abilities, lower ability of concentration and decision-making, as well as pseudo-dementia in severe cases. Despite numerous former studies on cognitive abilities, we do not yet have a comprehensive knowledge about the elemental neurocognitive changes typical of major depression. To partially fill this gap, here we review the studies related to the effect of mood and MDE on two main cognitive functions, namely WM and IL.

COGNITIVE FUNCTIONS AND MOOD

The quality and level of mental skills is determined by memory capacity to a great degree. The function of WM is to maintain and manipulate information during inference, understanding and learning, and it is composed of several modality-specific sub-systems. According to the widely accepted WM-model developed by Baddeley (1974) the phonological loop (i.e., verbal WM) is one of these WM-subsystems, responsible for the processing and storage of acoustic and phonological information, playing an important role in learning to read, understanding language and developing vocabulary (Baddeley, 2001). Another sub-system of WM is the visuospatial scratchpad (i.e., visuospatial WM), responsible for the manipulation of spatial and visual information and for the creation of imaginary pictures. With its assistance, we are able to orient ourselves through our environment (Baddeley, 2001). These are controlled and coordinated by the modality-free central executive. The central executive is responsible for response inhibition, focused attention, planning, information updating and decision making, which are also referred to as executive functions (Miyake et al., 2000b). In addition, the episodic buffer functions as a temporary storage of a multimodal code, connecting information from the various sub-systems and the long-term memory (Baddeley, 2001). The sub-systems also interact with one another in a vivid and complex fashion (Gruber et al., 2007).

The qualitative and quantitative performance of the various components or complex entities of WM is related to numerous measures (Miyake et al., 2000a; Gathercole and Pickering, 2000; Boone, 2007). In the case of healthy individuals, these components have a well-defined neuroanatomical background and are accompanied by with significant cortical activity (Gruber and von Cramon, 2001; Gruber and von Cramon, 2003; Koelsch et al., 2009). These studies showed that the prefrontal cortex (PFC), primarily dorsolateral PFC (Braver et al., 1997; Smith and Jonides, 1997) plays a critical role in WM functions. In addition, involvement of the anterior cingulate cortex (ACC) has been suggested especially in the case of WM-functions responsible for cognitive control and inhibition (Kiehl et al., 2000; Liddle et al., 2001; Peterson et al., 1999).

The cognitive performance can be influenced by such affective factors as stress, mood, and motivation. Stress influences the functioning of the body via specific biological and psychological paths, thus affecting the cognitive and affective functions as well as behavioural, immune and cardiovascular responses (Pruessner et al., 2010; Dickerson and Kemeny, 2004; Maheu et al., 2005; Lupien et al., 2007).

Some learning and memory functions rely on the hippocampus, the amygdala and the frontal lobe which feature high densities of stress hormone receptors, thus these functions can be easily influenced by stress (Lupien et al., 2007). The two major groups of stress hormones are the glucocorticoids and the catecholamines, which play a crucial role in the mediation of the effects of hypothalamus-pituitary-adrenal cortex axis (HPA) and in the stress response of the organism. In addition to the stress response, the secretion of glucocorticoids and noradrenalin is indispensable in the precise coding of high-arousal memories (Cahill et al., 1994; Maheu et al., 2004).

Stress and stress hormones can both have a positive or negative effect on cognitive functions, out of which their effect on WM, especially on executive functions, seems to be the most significant (Lupien et al., 2007). While some studies have come to the conclusion that stress enhances the performance of WM in test situations (Duncko et al., 2009; Weerda et al., 2010; Lewis et al., 2008), other results indicate that stress negatively affects verbal and spatial WM (Qin et al., 2009; Vytal et al., 2013). The effect of stress was noted especially in the early part of the tasks (particularly with regard to reaction time and accuracy) (Schoofs et al., 2008), while not being so significant in the later part of the tasks. Nevertheless, some studies have failed to show stress-induced decline in WM performance (Kuhlmann et al., 2005; Porcelli et al., 2008; Qin et al., 2009) and results suggest that the impact of stress on WM and executive functions depends fundamentally on individual's response (e.g. controllability) to stressors (Henderson et al., 2012).

The amygdala, the brain area most responsible for fear responses and memory encoding of events characterized with high-arousal emotions, plays an important role in the effects of mood on cognitive performance (LeDoux, 2000; Mather et al., 2006; Adolphs, 2008; Seymour and Dolan, 2008; Ehrlich et al., 2009; Roozendaal et al., 2009; Lupien et al., 2007). In addition, the neuroanatomy of mood and cognitive functions overlap in several areas (Cabeza and Nyberg, 2000; Phan et al., 2002). For instance, decreased activity of the dorsolateral PFC has been detected during the WM tasks in induced negative mood (Aalto et al., 2002; Gemar et al., 1996; Liotti et al., 2000; Mayberg et al., 1999). Nevertheless, contradicting results have evolved during the examination of how mood affects WM. According to the research of Gray (2001), while spatial WM improved in negative mood and declined in positive mood, verbal WM showed the opposite effect. In contrast, Chepenik et al. (2007) failed to find

significant effect of induced mood (independent of its valence) on WM, executive functions and attention. In addition, a more recent study showed that induced negative mood can cause attentional interference as a result of negative verbal stimulus on Stroop task (Isaac et al., 2012). Nevertheless, the majority of the behavioural studies as well as research showing that mood states with different valences involve different neural networks during WM tasks (Osaka et al., 2013) support the selective effect of mood on WM functions. Reviewing the effect of mood states on executive functions has also revealed contradictory results (van Wouwe et al., 2011; Phillips et al., 2002; Martin and Kerns, 2011), and the involvement of the central executive during tasks can improve the performance of attentional network in negative mood (Cohen et al., 2011).

These results suggest differential effects of various mood states on WM and executive functions, which may depend on the complexity of the task. In addition, the differences might stem from different mood inducers and tests applied as well as from the various ways of retaining mood.

BIOMARKERS RELATED TO COGNITIVE FUNCTIONS IN MDE

Most people experience a period in their lives when their mood is occasionally or permanently low. Depending on the level at which symptoms of this period disturb the body's affective regulation, we can talk about major depressive episode (MDE), as a clinical picture. MDE is accompanied by, in addition to affective dysregulation, a number of specific symptoms and neurochemical changes, such as poor sleep quality, lack of appetite, dispiritedness and other important metabolic, hormonal, endocrine and immune system related processes, which affect the cognitive functions at the same time (Villanueva, 2013).

Although the results of the functional and volumetric neuroimaging studies in MDE are partly inconsistent, a majority of studies suggests that the functioning of the hippocampus and the related orbitofrontal and prefrontal cortex, amygdala, thalamus and striatum are primarily affected in MDE (Bremner, 2005; Sacher et al., 2012). In addition, several neurobiological studies consider MDE to be a maladaptive response to stress, in strong co-occurrence with the dysfunction of the HPA axis (Strohle and Holsboer, 2003; Daban et al., 2005; Holsen et al., 2013). A typical accompaniment of affective disorders is the dysfunction of the hormone system, but it is questionable

whether MDE is the cause or the consequence of it (Villanueva, 2013). A typical hormonal alteration is the dysregulation of the stress hormones, including alteration in the blocking of cortisol production, increased levels of cortisol, increased excretion of cortisol and increased response to psychological stressors (Sher et al., 2013). An elevated level of cortisol can contribute to the impairment of executive functions (Egeland et al., 2005). Persistently high levels of glucocorticoids influence the natural cell formation in the hippocampus (Anacker et al., 2013), which contributes to the evolution of MDE and some of the disease-related cognitive dysfunctions.

Poorer sleep quality also accompanies affective disorders, thus in MDE as well, which is evident from the reports of patients and the sleep architecture measured by electroencephalography (EEG). The increased frequency of Rapid Eye Movement (REM) stages can be considered as a distinct biomarker of MDE (Steiger and Kimura, 2010) and distortions detectable by EEG in the sleep pattern starting from the 4th decade of life as opposed to younger people with depression (Lauer et al., 1991). Even though the sleep patterns of pharmacologically treated and non-treated patients show differences, changes of brain waves typical in MDE become more frequent as the state deteriorates. It has been revealed that in people with depression treated by antidepressants, while slow wave sleep (SWS) decreased and the length of REM stages shortened, the frequency of REM stages increased (Armitage, 2007; Kupfer, 1995). It is important to note that while many antidepressants decrease REM sleep and their effect on SWS is heterogeneous, these effects are more significant at the beginning of the medication process as opposed to its later segments (Wilson and Argyropoulos, 2005).

As a result of structural, synaptic and hormonal changes during MDE, the central nervous system is not, or only partially able to adaptively respond to the environmental stimuli. This maladaptive response necessarily leads to declined cognitive performance in MDE (Hammar and Ardal, 2009; Baune et al., 2010).

WORKING MEMORY IMPAIRMENTS IN MDE

MDE greatly influences the activity of the prefrontal and limbic brain regions, which can also be related to cognitive functions (Mayberg et al., 1999; Davidson et al., 2002; van Tol et al., 2011). The prefrontal cortex, which is responsible mainly for the executive functions (and other higher ordered cognitive functions), is also involved in MDE (Davidson et al., 2002;

Mayberg et al., 1999). The hypoactivity of the dorsolateral prefrontal cortex during working memory tasks has been recorded during MDE (Drevets, 1999). The middle regions of the prefrontal cortex, as well as the anterior cingulate cortex activated during cognitive control and inhibition have also shown signs of abnormal functioning in patients with depression (Bench et al., 1992; Drevets et al., 1992; Kennedy et al., 2001).

Impairments of performance related to WM in MDE have shown both mild (Landro et al., 2001) and severe (Egeland et al., 2003b; Taylor Tavares et al., 2007; Hinkelmann et al., 2009) forms. Even though these effects last regardless of the complexity of the task, they are more significant in the case of individual subcomponents (e.g. verbal working memory) (Gruber et al., 2011). Furthermore, MDE patients show a decreased cognitive performance in relation to executive functions, including shifting, planning and inhibition, which has been shown by studies investigating mental flexibility, verbal fluency and problem solving (Castaneda et al., 2008; Hammar and Ardal, 2009; Austin et al., 2001; Keilp et al., 2013; Gualtieri et al., 2006). Within executive functions, research has consistently shown severe impairment of inhibition and updating while performing semantic fluency tests in MDE (Calev et al., 1989; Trichard et al., 1995; Fossati et al., 2003; Grant et al., 2001; Ravnkilde et al., 2002; Den Hartog et al., 2003; Stordal et al., 2005; Markela-Lerenc et al., 2006; Gohier et al., 2009; Hammar et al., 2011; Hammar and Ardal, 2013; Harvey et al., 2004; Schmid and Hammar, 2013a). But see (Lyche et al., 2010).

When measuring WM in MDE, some characteristics of the illness have an impact on test performance. In WM tests, attention plays an important role, the dysfunction of which has proved to be a typical symptom of MDE (Landro et al., 2001; Porter et al., 2003), though mainly during tests which require a lot of effort (Barch et al., 2003; Egeland et al., 2003a; Cohen et al., 2001; Hinkelmann et al., 2009). In addition, attentional deficit is influenced to a great degree by the current affective state (MacQueen et al., 2002). A further key factor while measuring WM in MDE is processing of information, since one feature of MDE is psychomotor retardation (e.g. slower reaction time, slower processing of information) which is often measured by various tests (e.g. finger tapping task, Serial Reaction Time – SRT – Task) (Veiel, 1997; Naismith et al., 2003; Lyche et al., 2010; Keilp et al., 2013; Gualtieri et al., 2006; Den Hartog et al., 2003).

These deficits, in addition to being partly responsible for the symptoms of MDE, decrease the efficiency of mood control and the efficient tackling of depressive thoughts (Fossati et al., 2002; Kaiser et al., 2003), project the efficiency of pharmacological treatments (e.g. the executive functions) (Dunkin et al., 2000) and relapse-sensitivity (Schmid and Hammar, 2013b), thus requiring further examination.

FACTORS INFLUENCING COGNITIVE PERFORMANCE IN MDE

In spite of these results suggesting that the cognitive impairments of patients with depression form, from one side, a complete, steady and adequately structured picture, we are probably closer to the truth if we define cognitive dysfunctions as a heterogeneous and diffusive phenomenon. While in healthy individuals cognitive functions can be tied to well-defined neuroanatomical regions, in the case of psychiatric patients, they form a much more diffuse picture (Gruber et al., 2010; Henseler et al., 2009; Henseler et al., 2008).

When examining the results above, it is advisable to note several factors. One of these variables is that the above studies were conducted with a low number of participants. In addition, the heterogeneity of patient groups can also influence results, since psychiatric comorbidity seems to be the strongest predictor of cognitive performance impairment, thus explaining different results in MDE (Baune et al., 2009). Other clinical factors, such as the length of depressive episodes (Stordal et al., 2004) and their number, as well as age can also greatly influence cognitive performance (Porter et al., 2007). Although several results show that a depressive episode leaves a mark on the brain (Sheline, 2000) and the level of impairment of cognitive functions increases exponentially with the number of depressive episodes (Vanderhasselt and De Raedt, 2009), there are opposing results as well which did not find a similar connection in relation to executive functions (Lyche et al., 2010; Grant et al., 2001).

Cognitive performance is not independent of the severity of MDE either, though these results are also contradictory. While in some studies both working memory and executive functions (Austin et al., 1999; Hinkelmann et al., 2009; Baune et al., 2009), in other studies, neither working memory performance (Gruber et al., 2011) nor executive functions correlated to the severity of MDE (Porter et al., 2003; Schmid and Hammar, 2013a). As a result, the relationship between the severity of MDE and cognitive performance can-

not be regarded as clearly clarified (McClintock et al., 2010). Suicidal behaviour also affects cognitive performance, especially WM, executive functions and attention (Keilp et al., 2001; Audenaert et al., 2002; Keilp et al., 2013).

Attentional (Cassens et al., 1990) and motivational factors (Mialet et al., 1996; Elliott, 1998) can strongly influence performance via the level of effort applied to the test. At the same time, we can also mention the complex strategies related to attention, the increased involvement of which during the test can significantly impair performance (Thomas et al., 1999; Hammar et al., 2003). Furthermore, the partial or total absence screening for pharmacotherapeutic effects can also contribute to the diffuse cognitive results in MDE. This is supported by a study which examined the neuropsychological characteristics of MDE patients who were free of psychotropic and central nervous system activating medications and even though they showed several signs of cognitive impairments, for instance in the fields of memory, executive functions and attention, their psychomotor functions showed no discrepancy (Porter et al., 2003).

IMPLICIT LEARNING

Besides working memory, another important component of cognitive functions is implicit learning, which is the main focus our present review. Implicit learning (IL) occurs when the structure of complex stimuli or sequence of events in our environment is extracted without putting conscious effort into the process or realizing the learning process at all; later this unconsciously acquired knowledge can be implicitly applied in new circumstances (Cleeremans et al., 1998; Reber, 1993). The term explicit learning (EL) is used in the opposite situation when learning occurs with conscious effort, and the acquired knowledge can usually be declared, or verbalized (Sun, 2003). Implicit learning can be interpreted in an evolutionary paradigm as a mechanism of cortical plasticity (Reber, 2013); its intact functioning can contribute, for example, to our brain anticipating possible future stimuli through its implicit, automatic "predictive function" (Janacsek and Nemeth, 2012). At the same time, research has shown that IL plays an important role in learning our first language (Romberg and Saffran, 2010) or a second language (Rebuschat, 2013), in learning to play music or in perceiving music (Rohrmeier and Rebuschat, 2012), as well as in the case of social learning and social skills (Norman and Price, 2012). Furthermore, IL processes are less de-

pendent on attention as opposed to EL situations and WM tasks, which are greatly influenced by attention.

In addition to theoretical differentiation, these learning processes were thought to rely on different brain structures: EL processes were proposed to be highly hippocampus-dependent while IL processes were found to be primarily basal ganglia-dependent (Cohen and Squire, 1980). This picture has become more complex due to the functional studies in the past decades and shedding more light on the role of basal ganglia (Hikosaka et al., 2002) with regard to the striatum (Dennis and Cabeza, 2011; Rieckmann et al., 2010) and to its two structures, the nucleus caudate (Albouy et al., 2012) and the putamen (Hikosaka et al., 1999)). The cerebellum was also found to be involved in IL (Naismith et al., 2010; Doyon and Benali, 2005; Hikosaka et al., 1999). In addition, some studies also found hippocampus activation during IL, challenging the classical distinction between IL and EL processes and their neural correlates (Albouy et al., 2013b; Albouy et al., 2013a; Dennis and Cabeza, 2011).

It is empirically supported that explicit and implicit learning depend on different cognitive systems (Reber, 1993; Sun, 2003; Sun, 2007), and theoretically differ from one another in respect of several learning processes. The two different learning levels use two different types of representation and thus different degrees of access; plus two different types of learning methods. A further difference between the two systems is that if explicit learning is available first, learning will be top-down rather, while in the absence of it, it will be bottom-up. Finally, the so-called "action-decision" usually combines the recommendations of both levels (Sun, 2007). Complex learning processes require the harmonized functioning of several brain mechanisms, which often evokes parallel, interacting or competing relationship among the various memory systems and neural networks (Poldrack and Packard, 2003; Hardwick et al., 2013).

ASSESSMENT OF IMPLICIT LEARNING

Several tasks have been developed to measure IL. In these tasks the predictive structure that can be learned implicitly is present either in a covariation or in a temporal sequence of stimuli. For example, Artificial Grammar Learning (AGL) (Servan-Schreiber, 1990) belongs to the covariation tasks, where grammatically correct strings of letters are presented to participants without explicitly revealing the actual grammar rules. After practice, follow-up grammar tests have shown that participants acquire the rules without being able to consciously explain them. A key component of the acquired knowledge is bigram (a predictive pair of stimuli), which is the most simple relationship humans can learn such as 'TM', i.e. a chunk of two consecutive letters (Servan-Schreiber, 1990).

Another frequent covariation task is called Probabilistic Classification Task (PCL). In one specific type (Weather Prediction) participants are asked to forecast rain or sunshine based on non-weather-related pictures without any further instructions. There are usually four stimuli presented at the same time, and a configuration of a subset of these stimuli can predict weather outcome based on a probabilistic rule (Knowlton et al., 1994). Despite being unaware of this probabilistic configuration rule, participants' prediction performance improves with practice, that is interpreted as IL (Knowlton et al., 1994).

The most common task of measuring IL of sequences is the Serial Reaction Time (SRT) Task (Nissen, 1987), and its several modified versions. In the original SRT task, a stimulus appears in one of the four possible positions on the computer screen. Participants are told to press the response key corresponding to the location of the stimulus on the screen as accurate and as fast as they can. They are not aware of the fact that the order of the stimuli as they appear follows a predetermined, repeating pattern. With practice, participants become faster in responding to this repeating pattern, and they slow down when the pattern is removed from the stimulus stream (e.g., on a random block). Sequence learning is usually defined at the end of practice as the RT difference between sequence and random blocks (Janacsek et al., 2012).

In order to minimize the chance of participants to recognize the hidden sequence in the task, thus making the learning even more implicit, modified versions of SRT have been implemented. For example, Pedersen et al. (Pedersen et al., 2009) have included irregular stimuli patterns and distracting elements (i.e. arrows instead of stars). Another modified SRT version is the so-called ASRT (Alternating Serial Reaction Time Task) (Howard and Howard, 1997; Nemeth et al., 2010). In this task, random elements are inserted in the repeating pattern, creating an 8-element sequence in such a way that every second element in the line is random (e.g., 2r3r1r4r, where numbers corresponds to horizontally aligned locations on the screen, and r refers to randomly chosen locations out of the four possible locations). This structure is called probabilistic second-order dependency meaning that stimulus n can be predicted based on the stimulus

n-2 (e.g., 2_3, where _ refers to any location) but only with a 62.5% chance because other stimulus-triplets can also be formed due to the random elements (e.g., 2_1, 2_4, 2_2) in 37.5% of the time (Remillard, 2008). The former, more predictable runs of three consecutive stimuli are referred to as high frequency triplets and the latter as low frequency triplets (Howard and Howard, 1997; Nemeth et al., 2010). Because of these features, the ASRT task is capable of differentiating between sequence-specific learning and general skill learning in that sequence-specific learning is defined as the RT difference between responses to high and low frequency triplets, eliminating the potential confounding effect of a more general speed-up due to practice (called general skill learning) (Janacsek and Nemeth, 2012).

IMPLICIT LEARNING IN NEGATIVE MOOD AND AFFECTIVE DISORDERS

Implicit learning in negative mood

When the effect of mood on cognitive functions is examined, it is important to tease apart the specific influence of a less intense, positive or negative emotional state (i.e. mood) from more intense subjective experience of emotions and also from partly related experience of stress, since even though all these states tend to show similarities at several points, they are different in their origins and hence they might have different influence on cognitive functions (Lupien et al., 2007).

There were some studies examining the effect of stress on implicit and explicit learning. While explicit learning seemed to be impaired by experimentally induced stress or orally given cortisol stress hormones, IL have found to be less sensitive to these manipulations (Keenan et al., 1996; Kirschbaum et al., 1996; Lupien et al., 1997). Surprisingly, a recent study showed impaired performance on the SRT task after orally administered cortisol (Romer et al., 2011). They argued, however, that this deteriorating effect might be caused by participants' greater reliance on hippocampus-related more explicit processes (e.g., intentional search for a hidden pattern) while performing the SRT task, and these processes have been previously shown to be more affected by stress (Romer et al., 2011). Proving this hypothesis, a recent functional magnetic resonance imaging (fMRI) study showed that after stress induction participants switched from more explicit/declarative strategies to more implicit/procedural ones in the Weather Prediction Task

(Schwabe and Wolf, 2012). In addition, greater striatal activation was found during the task; moreover, the activation of the hippocampus negatively correlated with learning performance, suggesting that the more participants relied on hippocampus-related processes after the stressful episode, the lower their learning performance was.

Only a few studies have investigated the effect of mood on IL so far. For example, in the study of Pretz et al. (2010) participants performed AGL and SRT tasks in negative, positive or neutral mood induced by pictures from the International Affective Picture System (IAPS) (Lang P. J., 2005). They found improved learning in the AGL task in the negative mood condition compared to the other two conditions. Performance in the SRT task showed the same pattern, although it failed to reach significance. In a more recent study, participants performed the SRT task in negative or positive mood induced by music (Shang et al., 2013) and decreased learning was found in negative mood. Besides many, more subtle differences between the studies of Shang et al. (2013) and Pretz et al. (2010), different mood induction methods are one potential source for the dissimilar results by targeting separate affective pathways. Future studies are needed to disentangle these potentially confounding factors when examining the effect of mood on IL. Nevertheless, Thomas and LaBar (2008) have shown that there are prominent individual differences in how mood and related emotional processes affect learning performance. They used a modified version of the Weather Prediction Task. Participants were asked to predict whether they would encounter a snake or a spider in the woods. Those participants who reported fear of snakes or spiders exhibited a declined learning performance in the task. Interestingly, however, those participants who did not report fear of these animals, showed an improved learning performance that emerged on the second day of practice. This result highlights that the same emotional stimuli can have different effects based on the person's prepositions.

Implicit learning in major depressive episode

Implicit sequence learning is sensitive to frontal and subcortical damages, especially in the area of the striatum (Aizenstein et al., 2005; Exner et al., 2009; Exner et al., 2002). It is intact in the case of healthy individuals (Howard and Howard, 1992) and groups of patients where striatum is not involved in their pathophysiology (Martis et al., 2004). Sequence learning was impaired, however, in the case of diseases

where striatum is involved, for example Parkinson's disease (Jackson et al., 1995) and Huntington's disease (Knopman and Nissen, 1991). Since MDE is related to striatal grey matter volume decrease (Husain et al., 1991; Krishnan et al., 1992), and to a decrease in cerebral circulation and metabolism (Hickie et al., 1999; Drevets et al., 1992), sequence learning tasks can be useful theoretical tests for the functioning of striatum as well as ideal testers of the frontosubcortical model of depression (Naismith et al., 2006).

Research on implicit sequence learning in MDE led to mixed findings. Naismith et al. (2006) found decreased learning in the SRT task in patients with moderate to severe unipolar depression. Sequence learning performance negatively correlated with visuomotor speed, duration of depressive episode and severity of acute stress. Exner et al. (2009) went beyond this study by comparing melancholic- and non-melancholic subgroups of depression, and found lower sequence learning performance only in the melancholic group. In contrast, other studies showed preserved implicit sequence learning in geriatric depression (Aizenstein et al., 2005) and in patients recently remitted from depression (Pedersen et al., 2009).

It is important to highlight that in both cases where decreased sequence learning was found, results can be explained by the lack of a general speed-up in the task during practice (i.e., without an RT improvement of sequence blocks, no slowdown can be observed on random blocks). In a case study of a patient with cerebellar degeneration, Klivenyi et al. (2012) found the same pattern of no general RT improvement during the SRT task, and argued that in this case no conclusion can be drawn about sequence-specific learning measured as the RT difference between sequence and random blocks. In line with this argument, an fMRI study showed that cerebellum might be involved in the expression of sequence knowledge (Seidler et al., 2002); the sequence-specific learning itself, on the other hand, seems to rely primarily on the striatum (Sefcsik, 2009). Moreover, Naismith et al. (2010) found similar level of striatal activation in controls and patients diagnosed with depression, and concluded that the specific behavioural pattern on SRT task observed in the patients may depend on a more distributed neural network including frontal, temporal and cerebellar regions. Thus, the fact that MDE patients did not speed-up on the sequence blocks suggest difficulties in expressing the sequence-specific knowledge, but there is not enough evidence to conclude that the sequence-specific learning itself is impaired.

The consolidation of implicit learning in negative mood and in MDE

The previously described form of implicit learning occurs during practice, in the so-called *online periods*. However, implicit learning also happens between the practice sessions, in the so-called *offline periods*. During these offline periods the acquired knowledge is targeted by several biological and cognitive processes, rearranging and stabilizing the originally fluid memory traces after the initial encoding (McGaugh, 2000). One of the possible consequences of these processes is that memory traces become more resistant to interference after the offline periods, supporting long-term retention; moreover, performance can even increase compared to the end-of-practice performance (Robertson, 2009). The specific effect of mood is the different degrees of involvement of the learning systems and strategies (Schwabe et al., 2007).

To our knowledge, only two studies investigated the effect of emotional stimuli on retention of the implicitly acquired knowledge in healthy individuals. These studies presented neutral or arousing pictures with positive or negative valence from the IAPS database during the Weather Prediction Task, and found weaker learning performance in the arousal condition during the initial acquisition; nevertheless, long-term retention of the acquired knowledge was superior in the arousal condition compared to the neutral one, both after a 1.5-month and after a 3-month period (Steidl et al., 2006; Steidl et al., 2011). Note, however, that these studies were not designed to separately investigate the effect of negative or positive arousal on IL and retention.

We are not aware of any studies examining the retention of implicit sequence knowledge in depression. Dresler et al. (2010) studied the offline components of sequence learning in MDE, though they used the so-called fingertapping task, which is considered to rely at least to some extent on explicit learning processes of the sequence. They found no differences in learning performance between the healthy controls and the patients with depression during the online practice. After a 24-hour delay period, an offline performance improvement was found in the controls, whereas performance in the patient group showed a diverse pattern: patients older than 30 years of age showed no offline improvement, but patients younger than 30 years of age as well as patients remitted from depression performed similarly as controls. Nevertheless, future studies are needed to test whether a similar

pattern emerges in the consolidation of implicitly acquired sequence knowledge in depression.

CONCLUSION

In our everyday life we are constantly exposed to various events and conditions that can affect our mood. Research has been shown that especially negative mood and a depressive episode can have a great influence on cognitive performance, which, as a result of its particular characteristics, can be of predictive value during a pathological process, helping set up a diagnosis during clinical work. In addition, better understanding of the relationship between cognitive functions, such as working memory, implicit learning, and negative mood, MDE does not only help us understand the brain plasticity behind fundamental learning and memory processes but it also can contribute to the development of more effective therapeutic practices.

The relationship between explicit, conscious memory and mood is relatively well-explored, whereas the effect of mood on working memory and implicit learning received less attention. Here we aimed to give an overview of the existing literature on these less-explored fields. Research suggests weaker working memory performance in MDE and in negative mood, while studies of how affective disorders and mood affect implicit learning and consolidation yielded to contradictory results. In the latter case, further studies are needed to be able to tease apart some potentially confounding factors, such as general speed-up vs. sequence-specific learning, or learning vs. expression of the knowledge.

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A negatív hangulat és a major depresszív epizód hatása a munkamemóriára és az implicit tanulásra

A major depresszív epizód az egyik leggyakoribb pszichiátriai diagnózis, ami hosszútávú mentális és élettani következményekkel jár. A kognitív funkciók állapotának feltérképezése különösen fontos affektív zavarok esetében, mivel nem csak a betegek viselkedését, de a pszichoterápia sikerességét is befolyásolhatja. Emellett a hangulat és az affektív zavarok kognitív funkciókra gyakorolt hatásának vizsgálata segíthet megérteni az agyi plaszticitás és a neurokognitív hálózatok közötti összefüggést is. Míg az explicit, tudatos memória és a hangulat összefüggéseit elég jól ismerjük, a hangulat munkamemóriára és implicit szekvenciatanulásra gyakorolt szerepe kevesebb figyelmet kapott. A jelen áttekintő tanulmány célja az eddigi eredmények ismertetése ez utóbbi, kevésbé feltárt területek esetében. Összefoglalva, a kutatások arra utalnak, hogy a munkamemória teljesítmény csökken major depresszív epizódban, illetve bizonyos hangulati változások esetében; ezzel szemben az affektív zavarok és hangulat implicit szekvenciatanulásra gyakorolt hatásával kapcsolatos eredmények ellentmondásosabbnak bizonyultak, mely további kutatások szükségességére hívja fel a figyelmet.

Kulcsszavak: negatív hangulat, major depresszív epizód, munkamemória, végrehajtó funkciók, implicit tanulás, szekvenciatanulás, konszolidáció