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LETTER FROM THE EDITORIAL BOARD

Dear reader,

We proudly present the fourth edition of the Maastricht Student Journal of Psychology and Neuroscience (MSJPN). As opposed to the first three editions, this edition is not launched at the end of the academic year. The editorial board decided to issue editions of MSJPN a few weeks after the start of the academic year as this creates less workload and timing difficulties for both authors and reviewers. In addition, we believe that with the new release date we reach a larger number of students and we hope this will result in an even higher number of submitted articles.

The current edition comprises a total of 9 accepted manuscripts. Two of those are reports of empirical studies conducted by students at the faculty, and seven manuscripts are literature reviews. In MSJPN's 2014 edition the trend was set to provide the reader a cross section of the faculty. The 2015 edition has again accomplished to give the reader insight into the works of all our four departments. Moreover, several papers in our current edition show an interesting trend of covering cross-departmental topics.

MSJPN cannot exist without the input from authors. For the fourth year in a row we have been positively surprised by the number and quality of the submissions. We are very grateful to the students that have found the time and resources to write a manuscript and to go through the thorough review process of the journal. This review process is mainly conducted by students who have shown an unconditional effort to improve the manuscripts for eventual publication. We would like to thank them for that.

The journal continues to develop and to grow towards a fully student-led journal. Last year Laurien Nagels-Coune came to re-enforce the editorial board. This year, another student has become a full member of the board. We welcome Madeleine Dalsklev who, together with Laurien, as a section editor and has been responsible for all communications with authors, reviewers and designers.

As students become alumni, the journal would like to welcome new students to become members of the editorial board. Therefore, please contact any member of the board if you are interested in participating in the next edition of the journal.

The editorial board,

Anke Sambeth
Silke Conen
Laurien Nagels-Coune
Luís Tojo
Madeleine Dalsklev
Tim Leufkens

SCHADI EBRAHIMI

Burned-out surgeons – a review of risk factors and intervention types

Review

In today's society, many employees are affected by symptoms of burnout, which can be described as feelings of emotional exhaustion, depersonalization and ineffectiveness in the work context. Burnout rates are especially high in the intensive care environment, particularly in surgeons, as they appear to be confronted with high amount of workload and stress. In this paper burnout in surgeons is discussed, with special focus on different interventions that should be considered in preventing and intervening burnout. On the one hand, individual-directed interventions, focusing on improvement of individual coping with stress, are described. On the other hand, there are organization directed interventions, which tackle the stressors directly and have the capacity to reduce or eliminate them. Although individual- and organization directed interventions each have their respective shortcomings, increased use of organizational programs is suggested, as burnout results from the work context rather than being an personal issue. Even more, a combination of both strategies seems to be the best alternative to prevent and intervene burnout. Yet, more research is needed since there is a lack of well-designed studies of organizational and combinational interventions.
Keywords: burnout; surgeons; intervention; prevention

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INTRODUCTION

Modern work has undergone many changes as a result of environmental challenges, involving technological changes and global competition, thereby affecting employee

wellbeing (Landsbergis, 2003). Jobs were redesigned with the purpose that employees can handle the stressful effects, such as higher workload of downsizing (Mishra & Spreitzer, 1998) and experience intrinsic value from their job (Brockner et al., 2004). Yet, jobs became more demanding as workload increased and evoked exhaustion in employees, leading to health problems (Osthus, 2007). Burnout became an important issue through the course of these changes and is a syndrome that is characterized by emotional exhaustion, depersonalization and a reduced feeling of personal achievement (Maslach, Jackson, & Leiter, 1996). One occupation that appears to be mostly affected is the physical profession, in particular surgeons (Embriaco et al., 2007), who appear to experience more severe stress compared to other general occupational groups, but also compared to other medical practitioners (Klein, Frie, Blum, & Von dem Knesebeck, 2010; von dem Knesebeck, Klein, Frie, Blum, & Siegrist, 2010.) Burnout in surgeons is extremely high with several studies reporting a prevalence of burnout between 30-38% among American and European surgeons (Klein et al., 2010; Shanafelt et al., 2009).

There are several reasons why the surgical profession is stressful and intensive. Surgeons have to manage, among other things, high workload such as long working hours and high patient volume. This prevents surgeons from taking part in non-work events and spending time with family and friends (Shanafelt et al, 2009; Balch, Freischlag, & Schanafelt, 2009; Campbell, Sonnad, Eckhauser, Campbell, & Greenfield, 2001). The prolonged stress due to high workload can ultimately result in burnout (Maslach, Schaufeli, & Leiter, 2001).

The consequences of burnout are detrimental, as they can affect patient safety, can lead to absenteeism and turnover rates and appear to have mental consequences for surgeons, such as depression and drug or alcohol use (Shanafelt, Bradley, Wipf, & Back, 2002; Center et al., 2003). Therefore it is absolutely necessary for us to understand what can be done to counteract burnout. A wide body of literature already exists, investigating ways in which burnout can be reduced or eliminated in the workplace. One can divide intervention types into programs that focus on the individual, with the main purpose of increasing strategies to cope with stress, or in programs focused on the organization, which in the best case remove or reduce stressors directly. Yet, organizational programs aim for increasing productivity and quality of the organization, resulting in decreased burnout rates as a favorable side effect (Schaufeli & Enzmann, 1998). Although each intervention type has its advantages and shortcomings in preventing or reducing burnout, researchers suggests the use of both intervention types in order to efficiently reduce or remove burnout (e.g. Maslach et al., 2001; Awa, Plaumann, & Walter, 2010), which will be discussed further in this paper.

This paper is focused on answering two key questions: 1) What are the causes of burnout in surgeons? 2) Which type of intervention is the best in preventing or reducing burnout in surgeons? Although recent research has made some suggestions, a more detailed review on the causes of burnout in surgeons and a thorough comparison of the different intervention types on a more global level is lacking. In this paper, an attempt is made to find the most critical risk factors of burnout in surgeons and based on these factors the most relevant and studied intervention programs are considered. This will be done by (a) providing general

information about burnout, (b) explaining why surgeons are prone to burnout, (c) describing and comparing the different types of interventions that can generally reduce or eliminate burnout and (d) introducing strategies suggested by different authors that might prevent or reduce burnout in surgeons on both individual and organizational level.

METHODS

Literature Search

In this review a systematic search of burnout interventions for surgeons was conducted in electronic databases such as "Google Scholar", "PsycINFO", "Catalogue UM" and "PubMed", restricting the search to English and German studies. This was done during a period starting in November 2013 and lasting until June 2015. This review involved, among others, key words such as "burnout", "work stress", "surgeon burnout", "surgeon stress", "physician burnout", "intervention burnout", "individual burnout intervention", "person-directed burnout intervention", "organization-directed burnout", "organization burnout", "burnout prevention" and "stress management surgeons". Further, reference lists of different articles were analyzed as well as electronic books by searching for articles including above-mentioned terms in databases such as "Catalogue UM" and "DawsonEra".

BURNOUT

Definition and consequences

The most widely accepted definition of burnout is by Maslach et al. (1996), who characterized burnout along three dimensions: (a) Individuals suffering from burnout feel emotionally and physically exhausted, which means that they lack energy and are unable to interact with people, nor are they able to adequately perform ascribed tasks. (b) They feel cynical toward their job and the people they encounter on a daily basis. They disengage from work, participate less in work affairs and use this attitude mostly to protect themselves from exhaustion. And (c), people feel ineffective, meaning that they are less confident and feel deficient. These three dimensions are often measured by using the Maslach-Burnout-Inventory (MBI).

Burnout can also be defined in stages; most definitions claim that the early stages of burnout develop as a result of a misfit between people's ideals and real-life. This stress might lead to emotional exhaustion and changes in perception of one's job and colleagues, eventually leading to burnout. The development of burnout depends on individual's preexisting coping strategies. Those with weak strategies might be more prone to the development of this syndrome (Schabracq, Winnubst, & Cooper, 2003).

Although burnout can be the result of chronic job stress, these two concepts should be kept separate; whereas occupational stress evolves from a discrepancy between job demands and individual's resources, burnout can be seen as the last

stage resulting from a long-term exposure to such discrepancy, thus as the last stage of long-lasting job stress (Brill, 1984). When having burnout, people develop negative attitudes towards people they are working with, towards their job and the organization, which is not necessarily the case with job stress (Schaufeli, Maslach & Marek, 1993). Lastly, apparently only those people who started their job with high goals and expectations towards their job end up having burnout, whereas everyone can experience stress (Pines, 1993).

The consequences of burnout are broad and have been related to physical, mental and social outcomes and of course, the work situation. Physically, burnout can lead to problems such as headaches, gastrointestinal illness, or sleep disturbances (Kim, Ji, & Kao, 2011). Mentally, it has been found to be correlated to, among other problems, depression, anxiety and sleeping problems (Peterson et al., 2008). Sometimes burnout can also decrease social interactions and social relationships, in particular when work interferes with family issues (Singh, Suar, & Leiter, 2013). At the workplace, burnout can turn into absenteeism and decreased job satisfaction (Ybema, Smulders, & Bongers, 2011). It is also related to turnover in organizations, probably as people feel less committed to their employer and decide to leave their job (Visser & Rothmann, 2008).

General risk factors of burnout

Since burnout has such numerous negative consequences on life aspects, it is necessary to analyze the risk factors of burnout, such as individual characteristics. Regarding personality characteristics, a meta-analysis by Swider and Zimmerman (2010) has revealed high correlations between some of the personality dimensions and burnout components. In particular people high on Neuroticism and low on Extraversion, Agreeableness and Conscientiousness seem to be prone to burnout regarding all three burnout dimensions. In addition to these traits, Alarcon, Eschleman and Bowling (2009) found that, among others, characteristics such as low hardiness-levels, as well as low levels of self-esteem and self-efficacy, an external locus of control and low optimism-levels are significantly related to burnout. Hardiness is defined by Kobasa (1979) as a personality of being able to deal with stressors and therefore of preventing to become physically or psychologically ill, whereas external locus of control involves believing that one's success is driven by external factors. Lastly, concerning demographic variables, Brewer and Shapard (2004) found that younger individuals and individuals with less years of experience have a higher burnout rate.

The person-job mismatch theory

Although significant correlations between individual factors and burnout have been found, burnout appears to be mostly related to situational factors and therefore it should be analyzed and defined more in a social context, in particular in the work context (Maslach et al., 2001). Some job characteristics, for instance high workload, lack of social support, feedback and autonomy are related to burnout. According to Maslach et al. (2001), burnout can be defined as a chronic discrepancy between

individual resources and job demands. Thus it is considered as a misfit between individual and situational factors; the greater the gap between individual resources and work demands, the higher the possibility of experiencing burnout, whereas the better the match, the more individuals engage in work.

The assumption of a misfit or match is in line with the Job Demands-Resources (JD-R) Model by Bakker and Demerouti (2007), focusing on two critical components for employees: job demands and job resources. Whereas job demands lead to stress reactions and negative consequences for wellbeing, job resources (such as control, participation in decision-making and task variety, but also social support) lead to work motivation and engagement. Accordingly, high resources can have a buffer effect on the effect of demands on stress reactions, meaning that they can reduce the negative influence of job demands (Demerouti, Bakker, Nachreiner, & Schaufeli, 2001). In their comprehensive job-person fit model, Maslach et al. (2001) argue that burnout is expected to develop from the mismatch of job demands and job resources in one or more of six different areas: workload, control, reward, community, fairness and values.

In the first area, *workload*, individuals are said to experience a mismatch when work demands exceed individual resources. Requirements of the jobs might not be met due to lack of time, organizational support or expertise. The resulting resource depletion appears to be highly related to emotional exhaustion, as overload can deplete individual's energy levels.

Control describes the area where individuals might not have sufficient authority and the freedom to make decisions at work. This area is based on the Demand-Control (DC) Model of Job Stress developed by Karasek and Theorell (1990). The authors argue that when a job is highly demanding and at the same time employees have low control, the employee will experience strain. However, having control in a highly demanding job is argued to serve as a "buffer" against experienced strain and protects the employee's wellbeing. For example, a barista who can decide how to make the coffee, whereas he/she has time pressure for serving the coffee, might experience less stress due to his/her control on the actions she makes at work.

Reward involves the missing compensation for one's accomplished work and can include monetary rewards, but also recognition by others such as positive feedback by customers or colleagues. In terms of the latter, Buunk and Schaufeli (1993) argue that when individuals invest in a relationship, they hope to receive proportional gains from the recipient. When they experience an imbalance, their resources are drained and they feel emotionally exhausted. An imbalanced reward-system is often related to feelings of inefficacy because employees often feel less valued (Maslach & Leiter, 2008).

Moreover, *community* describes an area where positive social interactions at work are missing. It also includes social support, by supervisors or colleagues, which when considered as a personal resource in the JD-R Model, could buffer against many stress-related components of the job.

Fairness issues arise when specific aspects of the job are judged as unfair, such as workload, payment or promotion decisions. These perceptions can be emotionally exhausting and may lead to cynical attitudes towards one's work.

Lastly, *value* conflicts can be a major problem when there is a misfit between

individual and organizational values, as they are often not aligned. An example could be that employees enter a job with different career expectations than held by the organization (Maslach & Leiter, 2008). These five areas have been found to be the most critical determinants of burnout in general and, as will be illustrated later in this paper, are as well critical risk factors for surgeon burnout.

BURNOUT IN SURGEONS

Burnout prevalence in surgeons and consequences

Burnout rates in surgical occupations seem to be particularly high compared to other occupations (Klein, et al., 2010). In a study conducted by Yost, Eshelman, Raoufi and Aboulijoud (2005) in the USA, 38% of transplant surgeons were identified with burnout. In a later, comparable study, Shanafelt et al. (2009) conducted one of the largest studies of burnout in the USA among surgeons in 2008 and found burnout rates of 40%. The prevalence of burnout in surgery is not restricted to the USA; high burnout rates were found in several European countries. For example, in the UK in the same year, colorectal and vascular surgeons were analyzed for symptoms of burnout. Among them, 32% had high burnout rates on at least one dimension of the MBI (Sharma, Sharp, Walker, & Monson, 2008). Furthermore, Klein et al. (2010) found that 48.7% of German general surgeons suffered from burnout. An overview of different burnout rates in the USA and Europe among surgeons of different specialties can be found in table 1.

Table 1: Prevalence of surgeon burnout in different specialties in the USA, UK, Switzerland and Germany

Author/Year of inquiry	Country	Prevalence	Sampled population
Yost, Eshelman, Raoufi, & Aboulijoud /2005	USA	38% on emotional exhaustion	Transplant surgeons
Shanafelt et al./ 2008	USA	40%	Surgeons in general
Sharma, Sharp, Walker, & Monson/ 2005	United Kingdom	31% emotional exhaustion	Colorectal and vascular surgeons
Businger, Stefenelli, & Guller/ 2010	Switzerland	35% moderate levels of burnout	Surgical residents and surgeons in general
Klein, Frie, Blum, & Knesebeck/ 2008	Germany	48.7%	Surgeons in general

Some differences have been found in burnout rates in surgeons within different specialties; higher risk was observed in trauma surgeons, who reported the highest workload, followed by urologists (focus on urinary tract and reproductive system, otolaryngologists (focus on head and neck surgeries), vascular surgeons (focus on arteries and veins) and general surgeons (Shanafelt et al., 2009; Balch, Shanafelt, Sloan, Satele, & Freischlag, 2011). There is a small difference in burnout rates across different specialties. It is assumed that those physicians who are in frequent contact with chronically ill or dying patients are more prone to burnout (Shanafelt et al., 2009).

The consequences of surgeon burnout are broad and can, most critically, affect patient safety. Burnout is related to higher risks of medical errors, yet the correlational nature of the study does not allow causal statements (Shanafelt et al., 2010). Organizations may also be affected as employees with high burnout levels appear to leave their job for another practice or may retire early (Campbell et al., 2001). At a personal level, burnout can lead to mental illnesses such as depression, anxiety and sleep disorders (Center et al., 2003). It can destroy relationships, lead to alcohol and drug addiction, and to suicide (Oreskovich et al., 2008; Dyrbye et al., 2008; Lutsky et al., 1994).

Risk factors of burnout in surgeons: Applying the person-job mismatch theory

An analysis of recent research reveals some specific factors to be prevalent in most of the surgeons. Some individual factors, namely personality variables, are related to surgeon burnout; those surgeons who are idealistic, perfectionists and passionate about their work appear to be more at risk for burnout (Bittner, Khan, Babu, & Hamed, 2011). Yet, the most strongly correlated to surgeon burnout are high workload, problems managing work/family issues and lack of reward or autonomy. All these factors are related to the work context (e.g. Shanafelt, 2009; Balch et al., 2009; Campbell et al., 2001). Although the consequences of these work characteristics for each individual depend on individual characteristics (Balch, Freischlag, & Shanafelt, 2009), these are the factors that have been found to be generalizable to the majority of surgeon occupations in all specialties. As explained above and proposed by Maslach and Leiter (2008), these risk factors should be analyzed as an imbalance between personal resources and work demands. Here four of the six above-mentioned risk factors of the person-job misfit model will be named as they fit to the surgical context, namely workload, control, reward and value.

Workload is the factor most strongly correlated to burnout in surgeons. As proven by several studies (e.g. Campbell et al., 2001; Yost et al., 2005; Rawlani et al, 2011), surgeons have to deal with overwhelming work, high patient volume and too many work hours or number of nights on call per week, and this has been argued to happen more in surgical occupations than in many other occupation (Bittner et al., 2011).

Furthermore, many studies confirm that one of the most relevant risk factors is the imbalance between personal and professional life (Yost et al., 2005; Shanafelt et al., 2001; Campbell et al., 2001). This is based on the assumption that surgeons

spend too much time in hospitals and have too little time for personal and non-work related activities, as well as for personal growths opportunities. Especially young students appear to have difficulties to handle the high workload and are not always capable to balance time for work and family. In many studies it has been proven that younger surgeons are more prone to burnout (Campbell et al., 2001; Shanafelt et al., 2009), and it appears that burnout already has an effect on medical students or surgical residents across different disciplines (Bittner et al., 2011).

Control has also been found to be one of the top risk factors related to burnout. Surgeons are often insufficiently involved in decision-making concerning work tasks or procedures, which is related to burnout (Campbell et al., 2001).
Another problem is the lack of reward; it was found that surgeons find their job often intrinsically unrewarding, tend to experience a lack of reciprocity by the patient and believe their services are not appreciated (Campbell et al., 2001; Bakker, Schaufeli, Sixma, Bosveld. & Van Dierendonck, 2000).

Value also plays a role as a risk factor for burnout; many surgeons have high expectations in the beginning of their career, hoping that after the hard training period and the exhausting work hours they will understand meaning behind their work and eventually feel personally and professionally satisfied with their lives (Balch et al., 2009). Such an ideology is described in Psychology as "delayed gratification", defined as postponing immediate rewards and waiting for future rewards (Mischel, 1974). As these expectations are often not met and are in conflict with the organizational values (since the first years in practice are usually highly demanding), young surgeons become frustrated and distressed (Shanafelt et al., 2008).

The factors mentioned above appear to contribute to burnout separately, but they seem to be interrelated. In particular young surgeons have high expectations and "delay their gratification" of spending time with their family. Working for long hours (work load) and not having autonomy over one's schedule (control) might hinder surgeons to find a balance between work-family issues, such that their strategy of delayed gratification is even maintained after the training period(Balch et al., 2009).

Another problem is that many surgeons do not know that they have or are at risk of burnout. In a recent study by Shanafelt et al. (2014) surgeons in the USA were told to assess their own wellbeing compared to the wellbeing of their colleagues. Results showed that those surgeons, whose wellbeing scores were low compared to other surgeons, thought they would belong to the average or above. Many surgeons are thus not aware of how much their wellbeing is affected by distress and they do not seem to know that they are in need of a change. However, after receiving individualized feedback about their state, the need for change was recognized and half of the participants reported that they had the intention to make a change.

Other surgeons, but also physicians in general, believe that distress and burnout are normal and have to be accepted. They tend to ignore their own health as caring for the patient is prioritized; hence they do not seek help from others. Given this train of thought, they rather deny stress rather than confronting it (Shanafelt et al. 2014). This accumulation of stress might lead to symptoms of burnout.

BURNOUT PREVENTION AND INTERVENTION

Many different intervention programs exist in order to prevent and combat burnout. These can be individually-directed or directed at the organization. At the individual level, the focus is on teaching the individual to generally cope with stress. The aim is to make the employee more resistant to job specific stressors. Most of the intervention programs are situated on this individual level (Schaufeli & Enzmann, 1998). Organizational interventions usually have influence on work procedures and the organizational or social environment, in a way that they can reduce or eliminate stressors at work (Korunka, Tement, Zdrehus, & Borza, 2010).

Individual-focused interventions

Interventions, which focus on the individual, aim at heightening individual awareness of the situation, or attempt to reduce the arousal individuals often feel when experiencing stress. An example of awareness-promoting interventions is self-monitoring, which helps to focus on the symptoms of stress, for example through stress diaries. Cognitive-behavioral techniques aim to change the perception of the individual towards stressful events so that one's feelings and behaviors are positively altered. Relaxation techniques are also used here, serving to reduce the arousal (Schaufeli & Enzmann, 1998).

The general techniques used to improve employee's health and take part in more productive coping behaviors appear to be particularly difficult for surgeons as the professional culture of physicians incorporates a philosophy of putting the work before personal life, other's needs before own needs and professional achievement before personal achievement (Shanafelt, Chung, White, & Lyckholm, 2006). As a response, some specific strategies have been suggested that help avoiding burnout and increasing satisfaction. In a study by Shanafelt et al. (2012) different individual wellness strategies were tested and related to burnout. The strategies that were related to low risks of burnout were finding meaning in one's work, having a philosophy of a balance between personal and professional life, concentrating one's attention on what is important in life and taking vacations. Furthermore, although a rarely used strategy, taking part in mindfulness training for self-awareness is suggested, which can lead to reduced burnout and increased empathy (Krasner et al., 2009).

With the aim to prevent burnout in surgical oncologists, Shanafelt et al. (2008) developed a five-step solution for young surgeons, which can be classified as an individual-directed intervention; he recommended that after evaluating if one has a "delayed gratification attitude", one should (a) determine one's values, (b) optimize one's own career, (c) define stressors, (d) have a balance between personal and professional life and (e) develop wellness strategies.

Considering the first step (a), it is important that surgeons identify their personal values or goals, which can be for example being a medical educator or a professional healer. Questions surgeons could ask are "Why did I choose to become a physician?" and "What do I like about my job?". Then (b), surgeons should evaluate which type of practical work and work setting is helpful in reaching their goals and

they should be aware that interests change during their career. It is also advisable to identify specific stressors they encounter during their practical experiences, such as frequent night or weekend calls or high patient volumes (c). Surgeons can manage these stressors by for example distributing administrative work among colleagues or discussing one's work with mentors. Particularly these first three steps can help finding meaning in one's work. Further, achieving a balance between personal and professional life (d) can be achieved when surgeons become aware that they cannot "have it all" but are confronted with a trade-off; they should acknowledge that choosing one aspect of life, such as work, might reduce the opportunity to spend one's fullest time for family, and vice versa. Finally, (e), it is suggested to deploy wellness strategies, which help to grow personally and use one's leisure time efficiently. These strategies have also been found to be effective in some studies and include activities such as spending time with friends and family, personal reflection , spiritual practices, taking care of one-self and hobbies (Shanafelt, 2004). These steps do not only appear to promote personal and professional satisfaction, but also prevent the occurrence of delayed gratification, as gratification does not have to be "delayed" when surgeons experience meaning in their work and find an appropriate balance between work and home.

Although individual-directed interventions are effective, several shortcomings should be mentioned. According to Maslach et al. (2001), individual-directed interventions only affect the exhaustion component of burnout, leaving out cynicism and personal efficacy. A probable cause of this is that individual- directed interventions aim to minimize negative arousal , but do not try to change negative attitudes towards the job; thus, there would be no influence on the cynicism component. These interventions also do not maximize professional work-related skills nor resources and, as a consequence, do not increase personal achievement (Schaufeli, 2003). Also, they appear to be ineffective in a workplace environment where individuals would naturally find it more difficult to manipulate work-related stressors as opposed to personal ones. Another critical shortcoming is the longitude of their effect. In order to assess the effectiveness of different intervention programs on burnout (person-directed, organization-directed and a combination of both), Awa et al. (2010) conducted a meta-analysis, in which they included professionals of different occupational fields. It was found that individual-directed programs in general had positive effects on reducing burnout, but this effect persisted only for six-months. This finding is congruent with the idea that burnout is more strongly related to situational factors, and therefore should be tackled at the work- and organizational level (Maslach et al., 2001).

Organization-focused interventions

Many individual interventions focus on teaching employees how to handle stress, but it is recommended to focus more on cultural and environmental factors leading to the development of stress (Shanafelt & Dyrbye, 2012). Therefore it is recommended to tackle the problem at the work- or organizational level. More precisely, it is suggested to achieve a balance between personal resources and work demands in all levels (Maslach et al., 2001); this would mean to find a balance between areas such as workload, work-family issues, control, reward and social support. Whereas

the first two could be classified as job demands, lead to strain and therefore should be reduced, the control, reward and social support represent job resources, can lead to motivation and engagement and therefore should be increased (Shanafelt & Dyrbye, 2012).

Organizational interventions have the capacity to survey, eliminate or reduce stressors encountered at the work place through different techniques. To monitor stress, stress audits or surveys are used to determine occupational stressors, such as stress resulting from interpersonal relationships. These help organizations to develop strategies to improve organizational effectiveness and promote employee wellbeing. As an example of burnout prevention, organizations try to improve the job tasks and work environment to minimize work overload. For example, jobs are redesigned to involve more responsibilities or become more challenging. Time scheduling helps to reduce working hours or time spent with recipients (Schaufeli & Buunk, 2003). To treat burnout when it already affected employees, psychosocial check-ups are recommended, meaning that burnout-levels in employees are defined and subsequentlz treated. Support groups are also often implemented, providing help to stressed employees (Schaufeli & Enzmann, 1998; Schaufeli & Buunk, 2003).

Some organization-focused interventions in the occupational field of physicians aim to reduce burnout. Dunn, Arnetz, Christensen and Homer (2007) developed an intervention based on the promotion of three organizational factors: providing physicians control (having influence and authority on one's work), order (efficient office design and professional staff) and meaning (satisfaction with their job) (Shanafelt & Derbye, 2012), all characteristics that could be classified as personal resources (Bakker & Demerouti, 2007). These factors were determined prior to the intervention, followed by the development of improvement plans. A decrease in exhaustion and an improvement of empathy and emotional connection was found. Yet, the study had a small sample, as it is the case with most of the organizational-focused interventions. Most studies are not properly designed as they have too small and non-randomized samples, or/and no follow-up data. Thus in order to implement change, more evidence-based organizational-based interventions are necessary (Shanafelt & Dyrbye, 2012).

There are several reasons why organization directed interventions are implemented less. Theoretically, in organization directed interventions, the source of the problem of burnout as an organizational issue is addressed. Since most of the interventions on this level are established with the purpose to improve productivity and quality of the organization, the root of the problem is not always removed (Schaufeli & Enzmann, 2008). Furthermore, these interventions are complex as they require the involvement of employees from different departments, are time-consuming and entail high financial costs (Schaufeli & Enzmann, 1998; Schabracq et al., 2003).

Some suggestions have been made concerning organizational interventions that might be helpful in order to decrease burnout in surgeons. First of all, what appears to be lacking is a short self-assessment tool that determines physician's distress level as compared to their colleagues, since surgeons are often not aware of their risk of having burnout (Shanafelt et al., 2014). A recommendation could be to provide more stress audits or surveys in order to check current stress levels of

surgeons or psychosocial check-ups. Secondly, concerning job demands, workload could be decreased through reduction of paperwork and introduction of more flexible time schedules for critical family events. One could also implement appropriate administrative support systems and mentors providing help in balancing work and life issues (Spickard, Gabbe, & Christensen, 2002).

However, as workload is hard to change and often not even under the control of the organization, alternative interventions have to be used. This leads to increasing or replenishing job resources to increase control in surgeons. The health care industry should provide surgeons more autonomy and growth opportunities. Concerning intrinsic rewards, organizations should provide an appropriate amount of time for physician-patient relations, while the physician-patient time should be just enough to limit workload consisting of too high patient volume (Morse, Salyers, Rollins, Monroe-DeVita, & Pfahler, 2012).

In regard to the organizational community, an effective team appears to reduce burnout. As found in a study by Willard-Grace et al. (2014), clinicians who established a team-based working system and focused on respecting as well as communicating with each other experienced lower levels of exhaustion. These results can be possibly accounted by the fact that a team-based working structure might help to delegate responsibilities equally and thereby decrease workload. The authors therefore suggest establishing specific rules and changing work roles and hierarchies to implement a team-based culture within clinicians.

Combination of person- and organization-focused interventions

Although there are many advantages of an organization directed intervention, this approach does not target individual coping skills. A combination of both strategies is the best way to combat burnout. Maslach et al. (2001) proposed the implementation of both strategies: an educational approach, which means teaching an individual how to improve coping strategies, as well as management changes, thus changing the work conditions in a way that employees value their work and feel rewarded for it. Although the effect of a combinational intervention program has not been studied yet in the fields of surgery, some researchers compared intervention types for their effectiveness on reducing burnout in a wide field of different occupations. In their meta-analysis, Awa et al. (2010) found that a combination of both programs (individual- and organization based programs) lead to longer-lasting reductions of burnout, compared to individual-based programs alone, as the effects lasted for about 12 months and more. Yet, only a few combinational studies have been analyzed in their meta-analysis due to absence of such programs, in particular in the surgical practice.

Alternatively, one could examine studies of combinational approaches implemented in fields outside of the physical occupation. Innstrand, Epnes and Mykletun (2004) conducted a combinational intervention for staff members working with intellectually disabled people. First different stressors at work were identified. Second different intervention strategies on both individual and organizational levels were implemented. The individual approach consisted of a voluntary exercise program to improve fitness and wellbeing in employees. On the organizational level, on the other hand, performance appraisals (providing feedback), reorganization

of working schedules and improvement of routines for new employees were implemented. Positive effects of reduced exhaustion were found, without finding effects on the other two components of burnout (depersonalization and personal accomplishment), probably as follow-up tests were conducted too early (two months after the study termination).

Although no well-designed combinational study for surgeon burnout is reported, some authors made suggestions, which are applicable to the surgeon context. To prevent burnout, a general strategy for both individuals and organizations should be to nurture wellbeing of physicians on emotional, psychological, physical and spiritual grounds and from the beginning of their career until they retire (Spickards, Gabbe, Christensen, 2002). On the individual level, suggestions were made for physicians based on the most successful practices to promote wellbeing: spending time with family and friends, taking part in religious or spiritual activities, taking care of oneself, finding meaning in one's work and more (Weiner, Swain, & Wolf, & Gottlieb, 2001). On the organizational level, the focus should be on creating personal values and allowing more control, which can be addressed by strategies such as measuring intrinsic and extrinsic values, creating mentoring programs, or involving physicians in shaping and controlling their environment (Spickards et al., 2002).

Several strategies have been proposed in this paper, yet, there are some general suggestions applicable to all interventions. First of all, what appears to be critical as a first step in all interventions is identifying job stressors (Murphy, 1995). After this identification, one can choose the stressors that are most severe and resolve these. When there are stressors (or mismatches) in one area, such as in workload, these stressors can be compensated by matches in other areas, such as when people derive meaning in one's work (Maslach et al. 2001). Lastly, no matter which type of intervention is used, it is important that employees participate in the process and top management is involved (Cartwright et al., 1996).

DISCUSSION

The aim of this paper was to (1) analyze the most relevant risk factors of burnout in surgeons and (2) compare different intervention types that prevent and reduce burnout. In doing so, this paper built on the proposition that burnout develops as a prolonged misfit between personal resources and organizational demands in the following areas: workload, control, rewards, community and values. Research on surgeon burnout has found common factors related to burnout; surgeons are confronted with high workload, problems managing work and life aspects, experience too less influence on their work and receive too little intrinsic reward. Moreover, many young surgeons incorporate a philosophy of delayed gratification. Some are unaware of their high burnout risk, while others ignore this fact.

The consequences of burnout have been found to be detrimental for the surgeons themselves, the patients, and the organization. Surgeon burnout is related

to drug and alcohol abuse, as well as to several mental illnesses. It has also been argued that surgeons with high burnout levels pose a threat to patients due to surgeon errors. On the organizational level, burnout appears to be costly as turnover rates and absence are prominent.

Concerning possible interventions to reduce or prevent burnout, three intervention types have been compared, namely individual-focused, organization-focused and combinational interventions. Individual focused interventions aim at increasing coping skills. Although these interventions seem to have positive effects on reducing emotional exhaustion, these effects are short-lived. As burnout appears to develop as a result from work factors, it is suggested to implement organization focused interventions to a greater extent than individual focused interventions, as they have the potential to reduce or even eliminate risk factors of burnout. However, they are implemented much less than individual-focused interventions due to complexity, time- and cost issues. Furthermore, the main goal of this type of interventions is to improve effectiveness of the interventions, such that improving employee wellbeing becomes a minor matter.

Eliminating or reducing burnout is even more probable when individual- and organization directed interventions are combined, in such a way that the individual's coping strategies are improved and stressors at work are directly tackled. Yet, such interventions are rare, especially in the surgical occupation. Nevertheless, specific strategies for the individual surgeons and for organizations have been suggested, which could be united in the future. On the individual level, these strategies involve creating meaning in one's work by defining personal goals and working in the field congruent with one's goals, as well as taking part in meaningful activities outside work. On the organizational level, strategies such as providing appropriate stress and burnout assessment tools, increasing autonomy in decision-making processes for surgeons, ensuring adequate patient-physician time and implementing support opportunities are suggested.

It is important to consider some limitations of this review. Proposals of strategies and interventions for surgeons made in this paper are based on survey-studies where physicians were asked for their strategy used, but have not been converted into actual implementations. To give evidence-based and valuable suggestions about the effectiveness of such strategies, actual interventions and well-designed studies on these interventions are necessary (Shanafelt & Dyrbye, 2012; Awa et al., 2010). Moreover, to find interventions for surgeons, the most common risk factors of burnout among surgeons were illustrated. Yet, there might be individual differences in their prevalence, and there are surely differences between various specialties (Balch et al., 2009). Therefore, some strategies and intervention suggestions might not be applicable to some surgeons, which is why a proper screening prior to the development of the interventions is recommended (Murphy, 1995).

The results of this paper could have useful implications for the future. As burnout is related to turnover and absence, health care organizations could save money by implementing interventions against burnout (Buchbinder, Wilson, Melick, & Powe, 1999; Misra-Hebert, Kay, & Stoller, 2004). Furthermore, patient care might be endangered as burnout is related to increased errors (Shanafelt et al., 2002), thus a proper intervention might decrease the prevalence of litigations

(Crane, 1998). Since research is lacking in precise intervention suggestions, this review might help other researchers to shed light on the issue and encourage them to investigate different intervention programs.

All in all, after analyzing the literature and previous research, surgeon burnout can be best combatted through a combinational intervention. Yet, as these types of interventions are scarce, it is recommended to focus on available strategies on the individual or organizational level specifically proposed to prevent or reduce surgeon burnout. More research on organizational and combinational intervention types in this field is necessary.

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HILMA HALME

Attention deficit hyperactivity disorder: Potential gateway to pathological gambling

Review

Introduction: A high prevalence of gambling amongst individuals with attention deficit hyperactivity disorder (ADHD) suggests a need for specialised early intervention strategies.
Objective: This review aims to analyse the relationship between ADHD and pathological gambling, and to identify the biological, psychological, and social predictor variables.
Methods: Literature was searched from PsycINFO and PubMed in reference to individuals with a history of ADHD symptoms and current gambling problems. In total, ten studies were included.
Results: The results indicate a strong correlation with the hyperactive-impulsive subtype of ADHD and internalising disorders in the development of pathological gambling. Furthermore, persistent ADHD was found to increase gambling behaviour severity.
Conclusion: There is preliminary evidence that ADHD could lead to a specific profile of gambling behaviour, which is not merely based on impulsivity but a more cohesive biopsychosocial model. However, more research is required on neurobiological variables before a causal relationship can be concluded.
Keywords: Attention deficit hyperactivity disorder, gambling, biological, psychological, social, predictor variable

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INTRODUCTION

Attention deficit hyperactivity disorder (ADHD) is a developmental neuropsychiatric disorder characterised by inattention, hyperactivity, and impulsivity (American Psychiatric Association, 2000; 2013). The symptoms are highly persistent with a prevalence of 4.4% (Kessler et al., 2006). A review on risky decision making in individuals with ADHD found that children and adolescents with ADHD, but not adults, demonstrate riskier decision making than healthy controls (Groen, Gaastra, Lewis-Evans, & Tucha, 2013). Similarly, adolescence is generally characterised with a high prevalence of risky behaviour, including gambling behaviour (Shead, Derevensky, & Gupta, 2010). Interestingly, ADHD was found to increase the likelihood for gambling behaviour in the youth population with a significantly higher prevalence rate of gambling in adolescents with ADHD (Derevensky & Gupta, 2004; Faregh & Derevensky, 2011). This is a serious problem because adolescent gambling can have severe future consequences, especially since an earlier onset predicts more severe gambling problems (Hardoon & Derevensky, 2002; Kessler et al., 2008). For example, social gambling initiated during adolescence has a higher probability of resulting in problem gambling than social gambling initiated in adulthood (Kessler et al., 2008). Thus, young individuals with ADHD are particularly disadvantaged due to their general predisposition for risky and impulsive behaviour, which lead to gambling experiences at an earlier age (Pagani, Derevensky, & Japel, 2009).

Gambling disorders are associated with financial, legal, social, and health consequences (American Psychiatric Association, 2013). These include but are not limited to high debt, employment difficulties, substance abuse, antisocial personality disorder, and suicidal thoughts (Breyer et al., 2009; Gupta et al., 2013; Kessler et al., 2008). A national comorbidity survey conducted in the United States found the prevalence of adult pathological gambling to be 0.6%, with a majority initiating gambling behaviour by 19 years of age (Kessler et al., 2008). In the Diagnostic and Statistical Manual for Mental Disorders 4th edition (DSM-IV), pathological gambling is categorised as an impulse control disorder due to high comorbidity being reported between pathological gambling and impulsivity (American Psychiatric Association, 2000; Carlton & Manowitz, 1992; Carlton, Manowitz, & McBride, 1987; Specker, Carlson, Christenson, & Marcotte, 1995). However, the aforementioned national comorbidity survey illustrated that pathological gambling is more significantly associated with comorbid disorders, such as mood disorders (OR=2.5-4.6) and substance abuse disorders (OR=3.9-5.8), than ADHD (OR=1.8; Kessler et al., 2008). In the new version of the DSM, the DSM-V, gambling disorders are relocated under substance abuse and addictive disorders (American Psychiatric Association, 2013). Nonetheless, Canadian and French samples have reported that up to half of the youth with gambling problems reported clinical levels of ADHD (Faregh & Derevensky, 2011; Romo et al., 2014). Similarly, studies have shown pathological gamblers to report a history of ADHD before the onset of pathological gambling (Carlton &

Manowitz, 1992; Carlton et al., 1987; Kessler et al., 2008; Rugle & Melamed, 1993; Specker et al., 1995). In addition, persistent ADHD has been suggested to increase gambling symptom severity (Breyer et al., 2009). Subsequently, to unravel the role of ADHD, it is essential to determine which variables may lead to problem gambling behaviour in individuals with ADHD.

The first studies on the correlation between attention problems and pathological gambling were conducted over 20 years ago (Carlton & Manowitz, 1992; Carlton et al., 1987; Rugle & Melamed, 1993). Using retrospective data, these studies showed that pathological gamblers reported higher levels of childhood behavioural and cognitive symptoms related to ADHD, especially impulsivity (Carlton & Manowitz, 1992; Carlton et al., 1987; Rugle & Melamed, 1993). However, clinical measures for ADHD symptoms were not applied within these populations of gamblers. Nevertheless, the previous findings led ADHD to be included as a risk factor in Blaszczynski and Nower's (2002) pathways model of problem gambling. The model proposes that "impulsivist traits", such as ADHD, together with emotional vulnerability, biological vulnerability, and ecological factors predispose to gambling related cognitions and behaviours, resulting in one of the pathways towards problem gambling (Blaszczynski & Nower, 2002). Consequently, the model implies that the role of ADHD in gambling behaviour is based on impulsivity. Since then, about a dozen studies have measured the link between ADHD and problem gambling, and a high comorbidity has been established (Breyer et al., 2009; Canu & Schatz, 2011; Clark, Nower, & Walker, 2013; Dai, Harrow, Song, Rucklidge, & Grace, 2013; Davtian, Reid, & Fong, 2012; Derevensky, Pratt, Hardoon, & Gupta, 2007; Faregh & Derevensky, 2011; Fischer & Barkley 2006; Grall-Bronnec et al., 2011; Pagani et al., 2009; Rodriguez-Jimenez et al., 2006). Still, not a single study has been able to conclude why. Thus, it is important to establish if a causal relationship exists between childhood ADHD and later life gambling problems by evaluating the possible mediating factors.

On the one hand, ADHD may cause a genetic vulnerability, interfere with cognitive and emotional processes, or cultivate a social environment, resulting in a unique profile of pathological gamblers with ADHD (Gupta et al., 2013). This causal relationship may be further mediated by ADHD symptom clusters, more specifically the three subtypes: predominantly inattentive, predominantly hyperactive-impulsive, or combined type (American Psychiatric Association, 2000; 2013; Gupta et al., 2013). On the other hand, gambling problems might only correlate with the high levels of impulsivity, which is not specific to ADHD, as proposed by the pathways model (Blaszczynski, & Nower, 2002; Specker et al., 1995). Hence, ADHD may have a causal or a mediatory role in gambling problems. Determining mediating factors is important for improving early intervention strategies and psychoeducation, while support for a causal pathway would emphasise the need for specialised treatment for individuals with gambling problems and a history of ADHD. Consequently, the aim of this review is to summarise the biological, psychological, and social factors that may predispose an individual with ADHD to develop gambling problems.

METHODS

Search strategy and inclusion criteria

A systematic literature review was carried out to assess the biopsychosocial predictors of problematic gambling in populations with current or childhood ADHD symptoms. The literature was searched for in PsycINFO and PubMed. The study selection procedure is illustrated in Figure 1. The keywords 'ADHD', 'attention deficit hyperactivity disorder' or 'attention deficit disorder' were combined with 'gambling' and pathology related keywords, such as 'pathological', 'problem' or 'behaviour'. The following selection criteria were used for inclusion of studies: written in English, human participants, a clinically valid diagnostic tool for ADHD symptom assessment, analysis of gambling behaviour, and examination of biological, psychological or social aspects in relation to both ADHD symptoms and gambling behaviour. The last criterion resulted in the highest exclusion as many studies did not conduct a joint analysis of ADHD symptoms and gambling behaviour in regard to the biopsychosocial aspects. Studies focusing on other neuropsychiatric disorders, for example learning disability with comorbid ADHD, were excluded. The reason for excluding these studies is the difficulty in concluding the role of the primary disorder. Articles including the word gambling in reference to a gambling task, such as the Iowa Gambling Task, which is used to measure decision-making and not gambling pathology per se, were also excluded. The reference lists of the included articles were used to find other relevant articles. Even though one article (Clark et al., 2013) does not report administering a clinically valid diagnostic tool for ADHD, it was included because the questions administered are replications of the DSM-IV criteria (American Psychiatric Association, 2000). After completion of selection procedures (Figure 1), 10 articles published between 2006 and 2013 were included in the review (see Table 1 for an overview of these studies).

Study selection procedure

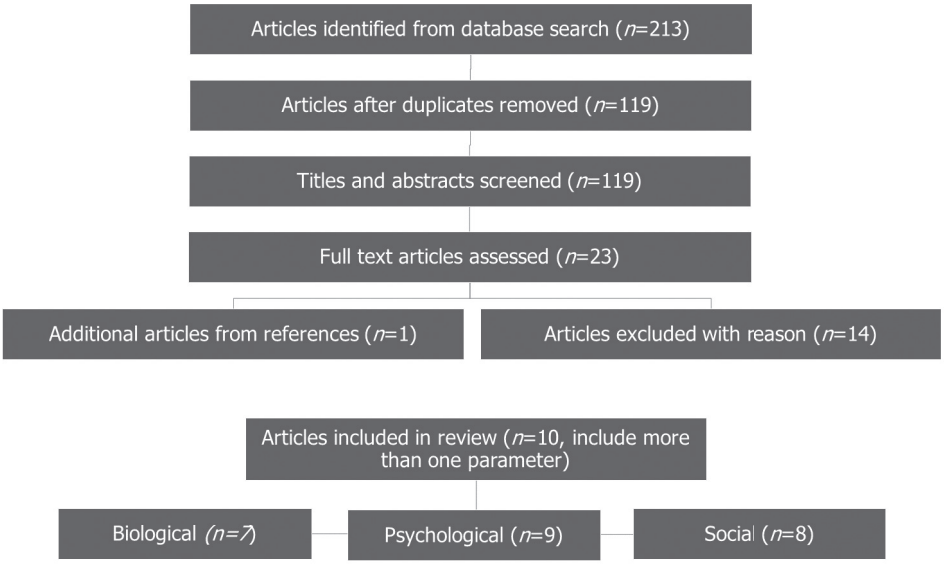

Figure 1. Flowchart illustrating the literature search procedure and articles included in the review for assessment of biological, psychological, and social predictor variables.

RESULTS

Only 1 out of 10 studies did not find a significant relationship between clinically relevant symptoms of ADHD and gambling behaviour (Canu & Schatz, 2011). Canu and Schatz (2011) found an increase in gambling behaviour amongst male, but not female, college students with high levels of ADHD impulsivity symptoms; however, significance diminished when only clinical levels of ADHD was assessed. This could be due to the subsequently small sample size (n=29), and thus ADHD subtypes could not be differentiated (Canu & Schatz, 2011). The results from another study are also questionable as a higher percentage of the ADHD group stated inability to control gambling than the control group, but the percentages were low, 6% vs. 1% respectively (Fischer & Barkley, 2006). Nevertheless, 4 out of 6 studies found that a history of ADHD increased gambling symptom severity (Breyer et al., 2009; Clark et al., 2013; Derevensky et al., 2007; Grall-Bronnec et al., 2011). In addition, one study demonstrated a higher prevalence of gambling problems in adults with persistent ADHD (since childhood) than adults with only childhood ADHD or adults without ADHD (Breyer et al., 2009). Adults with persistent ADHD also reported more severe gambling behaviour (Breyer et al., 2009). In the following sections are outlined the biological, social, and psychological aspects, which may contribute to the differences in findings.

Table 1. An overview of the studies assessed in the review.

Author (yr.)	Participants	*N*	Age (*M*)	Biological	Psychological	Social
Breyer et al. (2009)	Individuals with ADHD, Control group	235	18-24 yrs. (20.2)	Gender, IQ	ASPD, impulsivity	Education, employment, SES
Canu & Schatz (2011)	Individuals with or without symptoms of ADHD	224	18+ yrs. (20.3)	Gender	Impulsivity	Education
Clark et al. (2013)	Individuals with or without symptoms of ADHD	6145	18-27 yrs. (21.7)	ADHD subtypes	Emotional problems, gambling cognitions	Relationships
Dai et al. (2013)	Individuals with ADHD, Control group	60	17-64 yrs. (33.2)	Gender, IQ	Gambling cognitions, impulsivity	Education, SES
Davtian et al. (2012)	PGs with ADHD, PGs without ADHD	95	N/A (43.2 yrs.)	N/A	Personality (NEO-PI-R)	N/A
Derevensky et al. (2007)	Non-Gambler, Social Gambler, At-risk Gambler, Probable PG	2336	12-19 yrs. (14.8)	Age, gender, ADHD subtypes	N/A	N/A
Faregh & Derevensky (2011)	Individuals with ADHD and GP Controls with GP	1130	11-19 yrs. (N/A)	Age, ADHD subtypes	Depressive affect, emotional problems	Relationships
Fischer & Barkley (2006)	Individuals with hyperactive ADHD, Control group	239	19-25 yrs. 20.9	IQ	Inability to control gambling	Education, employment, relationships
Grall-Bronnec et al. (2011)	At-risk gamblers, PGs, Severe PGs	84	19-74 yrs. (41.8)	N/A	Comorbidities, impulsivity, gambling cognitions	Education
Rodriguez-Jimenez et al. (2006)	PGs with ADHD, PGs without ADHD, Control group	95	18-45 yrs. (32.7)	N/A	Impulsivity	Education, residence, employment

Note: ADHD=attention deficit hyperactivity disorder; ASPD=antisocial personality disorder; GP=gambling problem; NEO-PI-R=Revised NEO Personality Inventory; PGs=pathological gamblers; SES=socioeconomic status.

Biological

ADHD subtypes

Three studies measured the likelihood of ADHD subtypes in varying levels of gambling severity (Clark et al., 2013; Derevensky et al, 2007; Faregh & Derevensky, 2011). All studies concurred on probable pathological gamblers having a high prevalence of hyperactive-impulsive type. One study analysed hyperactive-impulsive type together with combined type ADHD (Faregh & Derevensky, 2011); however, combined type ADHD cannot be supported to have an effect on gambling behaviour (Clark et al., 2013). The findings on the predominantly inattentive type are controversial (Clark et al., 2013; Derevensky et al, 2007; Faregh & Derevensky, 2011). Derevensky et al. (2007) that the symptom severity of hyperactive-impulsive and inattentive type increased with gambling severity. Similarly, Faregh and Derevensky (2011) found a significantly higher prevalence of hyperactive-impulsive/combined type than inattentive type amongst at-risk and probable problem gamblers. In addition, Clarke et al. (2013) found the inattentive subtype to be a negative predictor of gambling problems.

Gender, age and IQ

Four studies analysed gender differences (Breyer et al., 2009; Canu & Schatz, 2011; Dai et al., 2013; Derevensky et al, 2007). Derevensky et al. (2007) found significantly higher scores on the hyperactive-impulsive ADHD scale for females than males as gambling severity increased. Nonetheless, individuals with pathological gambling behaviour and clinically relevant symptoms of ADHD did not differ in gender (Derevensky et al., 2007). This was the only study to come across any gender differences. Two studies measured age but neither found a confounding or mediating effect of age in the initiation of gambling, the severity of gambling behaviour or in ADHD symptomatology (Derevensky et al, 2007; Faregh & Derevensky, 2011). In addition, only one out of the three studies measuring IQ found a significantly lower IQ in the ADHD group (Breyer et al., 2009; Dai et al., 2013; Fischer & Barkley, 2006).

Psychological

Personality, impulsivity, and gambling cognitions

Davtian et al. (2012) found that adult pathological gamblers with ADHD had significantly more personality traits related with neuroticism, such as stress proneness, emotional instability and self-consciousness, compared to pathological gamblers without ADHD. They also reported higher levels of excitement-seeking and social discomfort. However, the two groups had similar levels of impulsiveness, which includes inhibition of impulses and resisting cravings (Davtian et al., 2012). Other studies are controversial about levels of impulsivity with one study supporting the previous statement (Breyer et al., 2009) and two suggesting gamblers with ADHD have higher impulsivity (Grall-Bronnec et al., 2011; Rodriguez-Jimenez et al., 2006). As aforementioned, one study found a positive relationship between impulsivity

and gambling severity in males, but could not confirm it within clinically relevant ADHD symptom levels (Canu & Schatz, 2011). Rodriguez-Jimenez et al. (2006) observed that pathological gamblers with ADHD are less able to delay gratification and they have lower inhibitory control than pathological gamblers without ADHD. Similarly, two studies found a significant correlation between a clinical diagnosis of ADHD in adulthood and gambling cognitions, such as the inability to stop gambling (Dai et al., 2013; Fischer & Barkley, 2006). This is also supported in individuals who reported childhood symptoms of ADHD (Clark et al., 2013).

Emotional problems and psychiatric comorbidities

Faregh and Derevensky (2011) found that adolescent pathological gamblers with ADHD had significantly more emotional problems than at-risk gamblers, social gamblers or non-gamblers with ADHD. In contrast, adolescent pathological gamblers without ADHD did not have a significant correlation between emotional problems and gambling problems (Faregh and Derevensky, 2011). Two studies have demonstrated that emotional problems were specific to ADHD populations, increasing the likelihood of pathological gambling (Clark et al., 2013; Faregh & Derevensky, 2011). In addition, ADHD correlated with higher negative affect amongst at-risk gamblers and pathological gamblers (Faregh & Derevensky, 2011). Likewise, Grall-Bronnec et al. (2011) found that the gambling and ADHD relationship is related to a significantly higher prevalence of comorbid mood, anxiety, alcohol abuse, and antisocial personality disorders. Another study supports the link with antisocial personality disorder (Breyer et al., 2009).

Social

Education, employment, socioeconomic status and residence

The two demographic variables that were found to be significant were education and employment, both with controversial findings. Fischer and Barkley (2006) found that the hyperactive group had a higher unemployment rate. Grall-Bronnec et al. (2011) found that gamblers with a history of ADHD were significantly less likely to have graduated from high school. This is supported by a lack of correlation between gambling and clinical ADHD symptoms in a college student population (Canu & Schatz, 2011). In contrast, Rodriguez-Jimenez et al. (2006) found no significant differences in education level or employment status.

Peer and family relationships

Three studies measured relationship problems (Clark et al., 2013; Faregh & Derevensky, 2011; Fischer & Barkley, 2006). Two studies found individuals with ADHD to report more relationship problems together with gambling behaviour than the control group (Clark et al., 2013; Faregh & Derevensky, 2011). Nevertheless, Faregh and Derevensky (2011) did not find family problems to be a significant covariate for gambling severity in individuals with ADHD.

DISCUSSION

The present review on the relationship between gambling problems and ADHD did not produce a coherent list of biological, psychological, and social variables, which would be agreed upon across the studies. This was not surprising within two as heterogeneous populations as problem gamblers and individuals with ADHD. Nevertheless, some variables received more support than others. Looking at the biological aspects, the hyperactive-impulsive ADHD subtype was most consistently associated with higher gambling problem severity, while differences in gender, age and IQ were not strongly supported as mediators in this relationship (Breyer et al., 2009; Canu & Schatz, 2011; Clark et al., 2013; Derevensky et al, 2007; Faregh & Derevensky, 2011; Fischer & Barkley, 2006). The lack of differences due to gambling initiation age was surprising as previous research on pathological gambling implied that an earlier age of onset results in higher symptoms (Hardoon & Derevensky, 2002; Kessler et al., 2008). Nonetheless, persistent ADHD was related to more severe gambling behaviour and a higher percentage of individuals with gambling problems (Breyer et al., 2009). This is an interesting combination of findings because adult (i.e. persistent) ADHD is commonly associated with inattentive symptoms and not hyperactive-impulsive symptoms (Hinshaw, Owens, Sami, & Fargeon, 2006). However, ADHD subtype was not differentiated amongst the individuals with persistent ADHD (Breyer et al., 2009). Consequently, this relationship should be further studied to unravel possible genetic predispositions.

As to psychological aspects, impulsivity was more controversial with two studies for higher impulsivity in individuals with ADHD and pathological gambling, and two studies against (Breyer et al., 2009; Davtian et al., 2012; Grall-Bronnec et al., 2011; Rodriguez-Jimenez et al., 2006). The findings suggested that the impulsive nature of individuals with ADHD and pathological gambling is caused by an inability to delay rewards and inhibit pre-potent responses (Grall-Bronnec et al., 2011; Rodriguez-Jimenez et al., 2006). This is supported by the main neurobiological dysfunctions in ADHD, which are thought to be the diminished prefrontal cognitive control and the reward related midbrain dopamine system (Groen et al., 2013). For example, children with ADHD were found to exhibit sensitivity for reward magnitude and frequency, preferring smaller rewards only when they were more frequent, while continuously disregarding punishment magnitude (Luman, Oosterlaan, Knol, & Sergeant, 2008). Furthermore, they chose smaller immediate rewards over larger future rewards (Luman, Oosterlaan, & Sergeant, 2005). Consequently, individuals with ADHD could result in a unique subgroup of problem gamblers due to their impaired reward system and developmental cognitive vulnerabilities.

A high prevalence of comorbid mood and anxiety disorders was found amongst individuals with ADHD and gambling problems (Faregh & Derevensky, 2011; Grall-Bronnec et al., 2011). This is supported by findings of emotional problems and neurotic personality traits, which increase vulnerability for mood and anxiety

disorders (Clark et al., 2013; Davtian et al., 2012). Similarly, personality traits of social discomfort explain the higher incidence of comorbid antisocial personality disorder (Breyer et al., 2009; Davtian et al., 2012; Grall-Bronnec et al., 2011). Internalising disorders are common comorbid disorders with ADHD and may be part of a causal pathway instead of mediating variables (Hardoon & Derevensky, 2002). Davtian et al. (2012) suggest that pathological gamblers with ADHD may use gambling as a way to cope with stress and negative emotions, similarly to gamblers without ADHD (Shead et al., 2010). This could be one reason as to why gamblers with ADHD were noted to experience an inability to stop gambling (Dai et al., 2013; Fischer & Barkley, 2006) – another reason being the aforementioned reward system impairments (Grall-Bronnec et al., 2011; Groen et al., 2013; Rodriguez-Jimenez et al., 2006). Hence, it is important to note that pathological gamblers with and without ADHD may differ in their reasons for gambling. Then again, the reasons are not mutually exclusive as serotonin and dopamine, associated with mood and reward respectively, are suggested to interact (Kenna et al., 2012). ADHD may therefore not only contribute to the development but also to the persistence of a gambling problem.

The only two social aspects with significant differences were education and employment (Canu & Schatz, 2011; Fischer & Barkley, 2006; Grall-Bronnec et al., 2011; Rodriguez-Jimenez et al., 2006). As Fischer and Barkley (2006) found gamblers with ADHD to have less likely graduated from high school, the non-significant relationship between ADHD and gambling behaviour in Canu and Schatz´s (2011) study could be confounded by the college student population. Moreover, obsessing about gambling has been found to cause school and work problems, which may lead to the lower education and higher unemployment rate (Breyer et al., 2009; Shead et al., 2010). Education level and employment status could therefore be mediating factors in the development of or consequences of an already existing gambling problem in individuals with ADHD.

In support of the DSM-V, in which gambling problems are no longer categorised under impulse control disorders, impulsivity is not causal to the development of gambling problems (American Psychiatric Association, 2000; 2013). Even though, the hyperactive-impulsive ADHD subtype is strongly supported as a mediator. Blaszczynski and Nower's (2002) model also located ADHD under "impulsivist traits"; however, the current findings suggest that ADHD should have its own place in the pathway towards gambling problems. Nevertheless, the other factors included in the pathway, such as the emotional vulnerability, are supported (Blaszczynski & Nower, 2002). As gambling disorders are currently categorised with substance abuse and addictive disorders, a connection could be expected (American Psychiatric Association, 2013). Conversely, a recent study in a Canadian sample found youth with ADHD to report more gambling behaviour compared to peers, but not substance abuse behaviour (Ostojic, Charach, Henderson, McAuley, & Crosbie, 2014). Then again, the gambling behaviour only trended towards significance (Ostojic et al., 2014). Nonetheless, individuals with ADHD seem noncompliant with current classifications, indicating that other domains of the hyperactive-impulsive ADHD subtype should be examined. These could include the mediating factors found in the current review, as illustrated in the biopsychosocial model below (Figure 2).

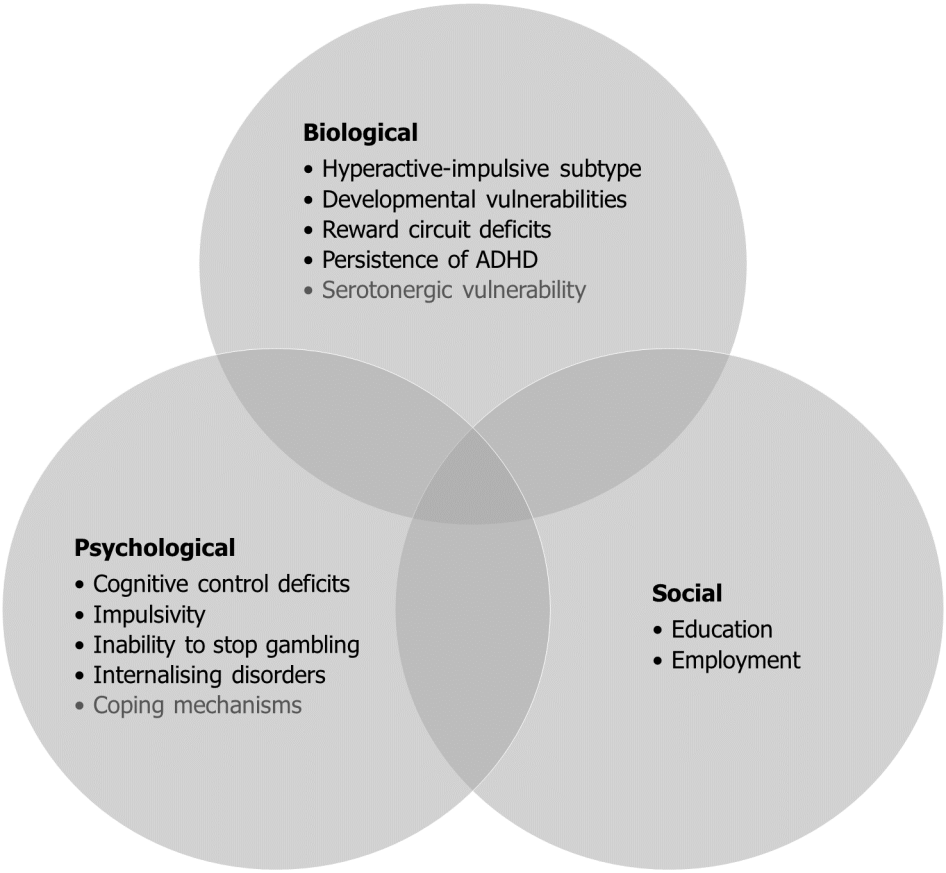

Figure 2. A biopsychosocial model of the variables that may lead an individual with ADHD to develop gambling problems, with the variables in grey proposed as future research.

CONCLUSION

The current review proposes a biopsychosocial approach to understanding the relationship between ADHD and pathological gambling. As shown in Figure 2, multiple variables have been suggested to increase the vulnerability for individuals with ADHD to develop gambling problems. However, most studies conducted on this topic, thus the majority of the studies included in this review, are cross-sectional studies. Consequently, they cannot conclude anything about causality between ADHD and gambling behaviour. Nevertheless, the two longitudinal studies imply that ADHD leads to gambling problems (Breyer et al., 2009; Fischer & Barkley, 2006). Based on the current results, the most prominent causal model for the development of gambling problems would incorporate an interaction between the hyperactive-impulsive ADHD subtype and internalising disorders, including negative affect, emotional problems and comorbid disorders (Clark et al., 2013;

Faregh & Derevensky, 2011). However, the causal relationship of this cannot be established before more longitudinal studies have been conducted. Nonetheless, a biopsychosocial approach can and should be used to establish early intervention strategies and psychoeducation of risky relationships, underlining that it is not simply impulsivity. As to treatment, the suggestion that pathological gamblers with a history of ADHD may have a different reason for persistent gambling than those without should be addressed.

Future research should focus on objective neurobiological factors, instead of only behavioural and self-report data. For example, individuals with ADHD and gambling problems may have a serotonergic vulnerability causing the impulsive behaviour, stress proneness and emotional problems (Davtian et al., 2012; Kenna et al., 2012). The promoter region of the serotonin transporter gene (5-HTTLPR) has been implicated in individuals with ADHD and comorbid internalising disorders, and could lead to a neurobiological link between ADHD and pathological gambling (Kenna et al., 2012). Especially, how it interacts with the dopaminergic system, and their joint effect on reward processing, cognitive control, and coping mechanisms (Groen et al., 2013). The findings reported in this review emphasise the need for an integrated biopsychosocial model.

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MIRIAM HEYNCKES

The predictive vs. the simulating brain: A literature review on the mechanisms behind mimicry

Review

Is it possible to understand the intentions of other individuals by observing their actions? And how does unconsciously mimicking the behavior of other people relate to this? Mimicry is an important element of social cognition. Its settings and effects have been well studied. However, the neurobiological mechanism behind it remains uncertain. This review illuminates two neuroscientific approaches to explain the mechanism behind mimicry. On the one hand, simulation through the mirror neuron system (MNS) describes mimicry as a by-product of simulation by certain motor-neurons. On the other hand, forward and inverse models, an internal prediction about future events, are an important concept in motor control theory and have been suggested to be involved in social cognition as well. The author proposes a model in which mimicry relates to forward and inverse models by acting as a facilitator of social cognition. A better prediction, due to mimicry, leads to a better understanding of others. Furthermore, limitations of the given approaches are illuminated.
Keywords: social cognition, forward models, mirror neurons, mimicry

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INTRODUCTION

One of the main aspects of being human is being a social individual. In the broadest definition, social cognition is what we think about ourselves and other people and how the processes involved influence our behavior and judgment in social contexts

(Hewstone, Stroebe, & Jonas, 2012). Social cognition as a research field has important sub-elements: for example the interest revolving around the Theory of Mind (ToM), the understanding and acknowledging of beliefs. Another element of social cognition and of importance to this review are social interactions. Interpersonal communication – the coordination between two interacting individuals – is one of the key features of social interaction. A complete picture of social cognition is far too complex for this review and therefore themes such ToM for an example are outside the focus of attention of this review. Interpersonal communication is about communicating information, meaning and feelings through verbal and non-verbal messages (i.e. gestures) and on the other hand, understanding intentions and messages from the other person. Accordingly the main focus of this review is on social interactions and mimicry.

Mimicry is an important element of interpersonal communication which can occur at non-verbal and subconscious levels. Mimicry reflects the similarity of behaviors during a social interaction. An example is the image of two women sitting in a café talking to each other and unconsciously sharing the same body postures while they talk. Both have the same leg crossed over the other and seem to be driven by the same idea when crossing their legs over again. This realistic example illuminates how omnipresent mimicry is. However, it still tends to go unnoticed most of the time. Particularly of interest is the finding that mimicry in social contexts leads to an increase in liking and vice versa (Chartrand & Bargh, 1999). It shows an important consequence of this ubiquitous but often unnoticed behavior. The effects of interpersonal coordination have been the topic of interest in a large amount of research. However, the larger role of mimicry when it comes to social cognition and understanding others' actions still needs further investigation. Therefore the focus of this review is to illuminate the mechanism behind mimicry by reviewing two approaches. On the one hand is the mirror system and on the other hand applications from predictive coding framework, namely forward and inverse models. Before reviewing these, a more thorough overview is given about what mimicry entails.

In general mimicry can be defined as "unintentionally doing what others are doing", and research has shown that it's often part of social encounters and occurs automatically (Hove & Risen, 2009). Mimicry was empirically observed for the first time in the 1970's in a study by LaFrance and Broadbent (1976). They observed students in a classroom and noted that automatic copying of laughter, movement, body posture and behavior is adopted several seconds after the observed original behavior, concluding that body postures function as non-verbal indicators of relations.

Furthermore, research during this time revealed a correlation between mimicry and liking (Lakin & Chartrand, 2003). Chartrand and Bargh (1999) demonstrated in a study that mimicry enhances rapport and liking. Within this study, a confederate mimicked the participants in one condition and strictly avoided mimicking them in the control condition. Mimicked participants reported liking the confederate significantly more than those participants not being mimicked. Experiments such as this study highlight the effects of mimicry on social coordination. In addition, recent research revealed that the relationship between mimicry and liking is bi-

directional; two persons who mimic the behavior of one another on a non-conscious level promote liking towards one another and vice versa. In other words, affiliations can be expressed through non-conscious mimicry (Lakin, Jefferis, Cheng, & Chartrand, 2003). However, mimicry can also have negative effects on affiliation (Bailenson, Yee, Patel, & Beall, 2008). Using computer agents that mimicked head movements of individuals confronted with them showed that explicit detection of mimicked movements had negative effects on affiliation.

Patients suffering from autism spectrum disorder experience many problems related to social cognition. A better understanding of the mechanisms behind social cognition is necessary to address and eventually alleviate these problems. The occurrence and effects of mimicry have been investigated thoroughly and a lot is known about the behavioral consequences. Nonetheless, looking at mimicry leads to asking why the human brain is sensitive towards the observation of other people's behavior. Answering this adds to the knowledge on social cognition. Therefore, this review has the objective to introduce two approaches explaining a mechanism behind mimicry.

The first approach concerns a topic that has received a lot of interest, with many supporters and as many people who disagree with the suggested concepts. Mirror neurons have received a considerable amount of attention since their discovery by Gallese and colleagues at the University of Parma. Since then many promising but also speculating hypotheses have been formed involving the mirror neuron system. While some researchers deny their importance in understanding other people (e.g. Hickok (2009)) other researchers strongly support the idea that mirror neurons enable humans to understand the meaning of other's actions (e.g. Gallese & Goldman (1998), Rizzolatti, Fogassi, & Gallese (2001)). Many researchers have investigated the mirror neuron system and argue that they function as the neural basis of human perception and action coupling and in a wider sense the understanding of actions and intentions of other people (Gallese, Keysers, & Rizzolatti, 2004). Therefore, it seems plausible to delineate how the MNS possibly relates to mimicry and to illuminate limitations of this approach.

Forward and inverse models have been shown to predict self-produced movement in the field of motor control. These prediction models often are also referred to as the predictive brain approach, the Bayesian brain or the predictive coding framework. They are gaining an increasing significance, reaching as far as describing predictive coding as the general principle of how the brain works. It is interesting to reflect mimicry from this perspective. The predictive coding framework basically states that large parts of information processing, namely perception, understanding and action (a great deal of what is happening in the brain) can be modeled and explained by predictions. Complex cognitive processes such as social cognition have been included in this framework (Brown & Brüne, 2012) and in this review the possible relation to mimicry is considered. Both approaches, the MNS and the predictive coding framework, are influential and a large amount of interest has been devoted to them. This leads to the question whether these two concepts from the field of neuroscience are able to explain mimicry, and which limitations they bring about?

PREDICTION VS. SIMULATION

Social cognition through the Mirror Neuron System

Gallese and Goldman (1998) introduced mirror neurons; a system of neurons partially located in the motor cortex. These mirror neurons fire when executing a movement but also when the person observes the very same movement. Gallese (2006) stated that "the hard problem in 'social cognition' is to understand how the epistemic gulf separating single individuals can be overcome" (p.2). The influential findings on the Mirror Neuron System (MNS) guided research strongly towards a future in which this problem will eventually be solved.

Research on macaque monkeys showed that mirror neurons are located in the ventral premotor areas in the cortex. They do not only respond to goal directed movements made by the monkey himself, but also when he solely observed or heard a performance of a similar action. This similar action could be observing how a nut is being picked up or hearing how this nut is being cracked (Gallese & Goldman, 1998). According to this idea, the monkey knew what the observed person was doing by using his own motor system (motor areas in the brain) as an internal simulator. Comparable findings have been also been made in humans (Fadiga, Fogassi, Pavesi, & Rizzolatti, 1995).

It has been suggested that the MNS could be the bridge between individuals, a neural mechanism that creates a social link (Gallese & Goldman, 1998). The activation of these cells creates the intuitive understanding of another person's actions that human take for granted when observing someone else. They are, according to Gallese, Keysers and Rizzolatti (2004), the neurophysiological basis of social cognition.

The "double-function" of mirror neurons refers to the ability of these neurons to fire when own movements are initiated, but also to fire when comparable movements are observed. This double- function enables to link 3rd-person experiences to 1st-person experienced events by simulating the neural event. This has been referred to as simulation by Gallese and Goldman (1998). This mechanism not only allows to see or hear what other members of one's species are doing, but enables an understanding in the observer as if he was experiencing the action himself. However, as discussed in depth in the limitation section a major weakness of this approach is that no empirical evidence has been found supporting how the mirror neuron system could accomplish action understanding.

Furthermore, the mirror neuron mechanism has been proposed to mediate the understanding of others' emotions. A study focused on patients suffering from epilepsy with an implanted electrode located in the insula. The insula is an area in the brain involved in the perception and experience of emotions, amongst one of them being disgust. Findings suggest that the anterior insula is active when perceiving disgusting odorants as well as when the person is observing the facial expressions of disgusted people (Krolak-Salmon, et al., 2003).

Relating back to mimicry the question arises how the MNS could relate to it

and what it contributes to the findings of increased social liking during mimicry. Gallese and Goldman (1998) showed that internally activated mirror neurons cause the execution of a planned movement. So to say, mirror neurons function as typical motor neurons. However, the very same mirror neurons when externally activated (i.e. when observing someone) show comparable activity but do not lead to an execution of the movement. They seem to be inhibited with regard to the usual self-initiated movement or as Gallese and Goldman call it "taken off-line". This seems counterintuitive, as there is neural activity in motor areas but no movement follows as a consequence. Gallese and Goldman (1998) concluded, that the MNS functions as a simulation mechanism to put the observer "into the same 'mental shoes' as the target".

A study by Fadiga et al. (1995) exploited transcranial magnetic stimulation (TMS) to stimulate the motor cortex of a subject. TMS is an established technique, which uses a strong magnetic field to stimulate certain areas of the brain. In this study the subject was observing hand movements grasping an object, while motor evoked potentials (MEP's) were being recorded from his hands. The researchers were able to demonstrate that this led to significantly higher MEP's in the same hand muscles, as the ones being observed. This condition was compared to conditions where the subject was only looking at the object or tracing the confederate's finger drawing geometrical figures in the air. This is further evidence supporting the idea of a human system that matches observing an action and the execution of the same action on a neural level. Comparable results were made with MEP's recorded from the tongue (Fadiga, Craighero, G.Buccino, & G.Rizzolatti, 2002).

The author suggests an explanation how mimicry could be the result of a mirror neuron system. Facilitated motor responses through the MNS then act as the basis of mimicry. Mimicry is essentially the unknown copying of an observed behavior, which comes into existence, as the necessary muscle groups used are facilitated, as explained in Fadiga's (1995) TMS study on MEP's. Motor responses are facilitated through the activity of mirror neurons in motor areas corresponding to the observed movement. Mimicry then appears to be a by-product of the simulation mechanism of mirror neurons. According to Gallese (1998) the purpose of mirror neurons is to serve as a simulator leading to action understanding of others. This is then accompanied by mimicry, which is essentially synchronized behavior (*for clarification purposes the author created Figure 1*). The given explanation entails that research investigating mimicry, was looking at observable instances of a simulation mechanism (the MNS). Simulation through mirror neurons is a form of neural synchrony between the observing person and the person performing an action and being observed. Self-other overlap refers to an understanding of another's intention such as putting oneself "into the same 'mental shoes' as the target" (Gallese & Goldman, 1998). Neural synchrony, by means of mirror neuron activity, thus leads to action understanding (a self-other overlap) and it leads to mimicry.

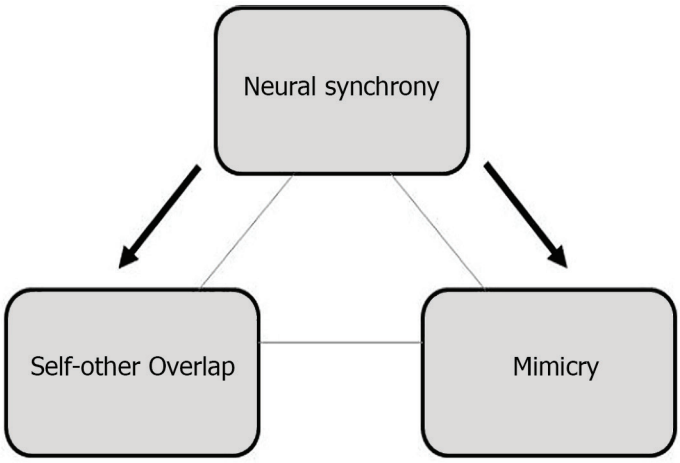

Figure 1. Simulation leads to an understanding of the other (self-other overlap) and to mimicry through facilitated motor responses

Wheatley, Kang, Parkinson and Looser (2012) state that the MNS evolved to function as a bridge between two individuals thus promoting social understanding. First they conclude that neural synchrony (MNS) is an efficient process, which is supported through its ubiquity of forms within the brain and the fact that simulation through mirror neurons leads to a self-other overlap reducing processing capacities. Efficiency of any kind in the long term sustains throughout evolution and is often naturally rewarded. Their second argument is based on similarity functioning as a cue of kinship. The broad concept behind kinship is that there is a kinship mechanism that favors social behavior towards relatives, due to evolutionary relevance, which leads people to be more comfortable with similar people. When mimicking behavior, the similarity in it, even if not perfect, functions as an implicit cue of kinship and this might lead to liking. In other words, shared movements suggest shared genes.

Finally, leading back to the introduction of this paper is the approach of looking at mimicry from the MNS viewpoint. Mimicry can be explained through the concept of the MNS. Within this approach mimicry is seen as a by-product of neural synchronization/simulation through the mirror neurons. These motor neurons fire when observing someone but no motor execution occurs due to inhibition of this neural command to move. Mimicry to observed actions occurs quite often. However, the link between MNS and an increased social liking through mimicry needs a stronger argumentation than currently suggested by the author. Wheatley et al. (2012) note that the critical point is, that neural synchrony (MNS activity) appears to ensure efficient processing by means of a rewards signal, which explains findings by e.g. Chartrand and Bargh (1999) on the link between mimicry and liking.

Limitations of the MNS approach

Mirror neurons are an important neurobiological discovery and have a strong intuitive appeal as to their importance for understanding social cognition. The MNS is often described with general explanations and functions which make it easy to understand and appeal as an explanation for many phenomena. However, empirical evidence for a concrete mechanism is lacking. Gallese (2006) stated that: [...] "We do not have a clear neuroscientific model of how humans can understand the intentions promoting actions of others they observe". And still eight years later the same question remains: if the MNS is in fact in charge of mediating understanding of actions and social coordination, how could it accomplish this?

Building onto this criticism are questions about the interpretation of fMRI data used to infer MNS activity. Gallese's and Goldman's (1998) initial study focused on single-cell recordings that specifically show the activity of certain neurons in the monkey cortex. However, how can we be sure that the activity measured in one voxel (which is by far not equivalent to one neuron) originates from the same neurons when observing action and when executing the very same, they could merely be neighboring cells.

Research has contributed a lot to specify where the exact parts of the MNS are located within the monkey brain and also partially within the human brain (Miall, 2003). However, this knowledge has often been oversimplified by the media and applied to many aspects of social cognition. Mirror neurons were claimed to create empathy when watching movies, leading to experience the same emotional moments seen on screen (dailymail.co.uk, 2013). Furthermore, in relation to the recent soccer world cup it has also been claimed that mirror neuron activity reflects higher understanding of the game. More experienced soccer players have higher activity of the MNS when watching a game (focus.de, 2014). However, there is no research that confirms the exact function of mirror neurons.

Research has shown that these cells are part of a complex interacting network of neurons. Also the category of what qualifies as mirror neurons is very large, comprising cells that fire when observing an action, hearing an action or seeing biological motion. Of these cells many fire only under very specific circumstances and others fire to a broad range of movements. (Gallese & Goldman, 1998).
Research is still at the beginning and the limitations stated earlier should be kept in mind. Generalizing from areas of the monkey brain to areas of the human brain should be done with caution and also using human brain imaging data has its disadvantages, as it cannot depict single neuron activity. Single cell recordings give more detailed insight into the functioning of the MNS. However, it is invasive and seldom done in humans; only if medically necessary.

A different proposal for a mechanism behind social coordination and eventually the understanding of others' intentions is the predictive approach of the brain, stating that the brain is able to predict events close in time. This mechanism has been suggested in the framework of the sensorimotor system and recent approaches focus on applying this concept onto social cognition. The following section illuminates on this.

Social coordination through internal models of forward and inverse planning

Forward and inverse models are established concepts within the Central Nervous System (CNS) to explain motor control in an individual. These models make use of a prediction of what a sensory event will be (Wolpert & Flanagan, 2001). The following section outlines forward and inverse models and their function in motor control. Furthermore, a link to mimicry is established by explaining social cognition through forward and inverse models.

Forward models of motor control

Research established a general acceptance of the concept of forward models in motor control and these forward models predict the sensory consequences of our executed movements (Wolpert & Miall, 1996). Forward models of the motor system use a neural copy of a motor command. This neural copy is referred to as corollary discharge and is used to establish a prediction of the position of the body. This prediction is then compared to the actual position of the body after executing the movement.

Using tickling as an example illuminates how this mechanism works and explains why you cannot tickle yourself. An internal forward model supports attenuation of self-produced movements by using sensory predictions of the motor system (Blakemore, Wolpert, & Frith, 2000). Accordingly, there will be actual sensory feedback from your hand; for example proprioceptive information, which is information about the relative position of your hand in space. Furthermore, there will also be the predicted sensory feedback from the forward model, which is established through the corollary discharge and called the efference copy. The discrepancy measured by your forward model between the predicted and actual feedback is what establishes the "tickliness" of someone. If there is no sensory discrepancy between your executed movement and the predicted movement then a sensory attenuation occurs and the sensation is not as tickling. This is what happens if a person tickles herself. However, if for example someone is being tickled, the efference copy of the self-created movement is missing. Accordingly this person cannot predict the movement and no sensory attenuation occurs, due to a high prediction error. In consequence being tickled is experienced as a lot more tickling in comparison to self-tickling. Blakemore, Wolpert and Frith (2000) propose that this attenuation through the forward model has advantageous effects for an individual as sensory information is being filtered. Filtering of information, especially of external sensory information is a necessary element of many brain processes to avoid a cognitive overload and ensure efficient processing of the environment. This filtering is an important trade-off between sensing everything and recognizing what is important to an individual in terms of survival. Sensory feedback created by external events can be more easily discovered and self-produced movements, which are filtered, can be weakened (Blakemore, Wolpert, & Frith, 2000).

Inverse models of motor control

Inverse models are, as the name suggests, an inverse model of forward models. Inverse models form the relationship between intended goals or actions, and the

motor commands to achieve those goals. So basically, inverse models use a given input to estimate an appropriate command. As an example, if you are hungry and intend to pick up a slice of apple, your internal inverse model transforms the visual input (sensory representation of relative positions of the apple and your arm) into motor commands. The flow of information along pathways in the brain would be from occipital visual areas to areas in the posterior-parietal cortex (PPC) and would then feed through pre-motor and motor cortex to execute the command (Miall, 2003).

It has been shown that forward and inverse models act together within the motor system to establish a functional motor control. This is achieved through the architecture of motor control that incorporates multiple pairs of forward and inverse models (Harumo, Wolpert, & Kawato, 2001). Functional motor control is achieved through a dynamic repetition of an inverse model giving a first command to move and a forward model calculating the error between the prediction of the movement and the actual position. This error is then fed back to the inverse model, which reacts with an upgrade command (Churchland, 2002). It follows that the combination of forward and inverse models presents a mechanism that is fast and reliable, an essential aspect of motor control. Constant monitoring through them allows correcting or reacting to unexpected events, such as lifting an object that is lighter than expected and motor responses occurring appropriately. And taking this concept one step further, assuming that forward and inverse models are capable of learning this combination of models would create a very efficient system able to acquire a broad range of sensorimotor skills and could be a fundamental mechanism for different cognitive functions (Churchland, 2002).

Social cognition through forward and inverse models

Forward and inverse models are not exclusively applicable to motor control. Forward and inverse models are a fundamental computational mechanism for sensorimotor prediction. This has been well researched and an increasing amount of attention and work is devoted to investigate how a predictive coding framework can include complex cognitive processes such as social cognition (Brown & Brüne, 2012). Research revealed a link between internal models of motor control and the understanding of one's own intentions (Blakemore, Wolpert, & Frith, 2000). The following section elaborates on this finding and illuminates how forward and inverse models function in relation to social cognition.

Research comparing schizophrenic patients with healthy subjects revealed important implications for the functioning of forward models. The efference copy of a movement is likely to have a more important role with regard to sensory attenuation than the re-afferent information from the body part being moved. A defect in the "self-monitoring" mechanism of the forward model that creates the sensory prediction of movements (the efference copy) causes schizophrenic patients to experience a passivity of their movements. This means they cannot distinguish between movements made by themselves or others through the sensory prediction that would attenuate the sensation. Healthy control subjects were compared to schizophrenic patients with symptoms of passivity. The subjects judged whether they tickled themselves or whether they were externally tickled. There was a clear

difference in tickliness between healthy subjects and schizophrenic subjects. Healthy subjects reported a difference in tickliness when tickling themselves or being tickled. However, schizophrenic subjects did not report this difference (Blakemore, Wolpert, & Frith, 2000). This reveals the possible importance of internal forward and inverse models in relation to social cognition. Understanding how humans can become aware of their own intended actions is the first step in comprehending how humans are capable of understanding others.

The author suggests a hypothetical predictive account initially suggested by Wolpert, Doya and Kawato (2003). Observing another person (here person 2) could function as visual input for an inverse model. The input replaces for example the relative position of one's hand and an object. Following this, an inverse model would generate communicative signals by initiating certain motor commands towards person 2 (e.g. speech gestures). A forward model of the individual would predict the sensory consequences of the motor command, in this case speech commands. Person 2 reacts to this by giving a motor command again, which closes the social interaction loop. His command provides feedback to the forward model of the first person; a prediction error is fed back to the inverse model which provides a new command through these consequences. As described earlier, a discrepancy between the prediction of another person's behavior and the actual observed behavior can be used to refine the inverse model (Wolpert, Doya, & Kawato, 2003). Furthermore, through an inverse model a person becomes aware of his intention why he wanted to move (e.g. pick up slice of apple). With feedback from the person being observed an estimate of what one's intention would have been for the same action can be inferred. This intention is then attributed to the person being observed (Blakemore & Decety, 2001). This social interaction loop functions by continuously predicting the other person. The following section illuminates how this social interaction loop based on forward and inverse models relates back to mimicry.

The human brain is all about efficiency. Communication between areas of the brain is created through synchronous firing of neurons in these areas. Also sensory input from the environment is processed in separate areas in the brain e.g. color and shape of objects are processed in different visual areas. These features of objects are combined again through synchronous firing (Engel & Singer, 2001). Neural synchrony in the brain is therefore an efficient process and the brain shows certain sensitivity to synchrony. This is also the case with mimicry. Mimicry of behavior promotes liking, on the other hand liking someone promotes this unconscious mimicry (Lakin & Chartrand, 2003). The author proposes that mimicry acts as a facilitator of social cognition. It is the result of interacting forward and inverse models of two or more persons respectively. Being in synchrony on a behavioral level (mimicry) promotes a synchrony on a neural level. This neural level refers to the prediction made by the forward models of two or more interacting persons. Understanding of others' intentions is promoted through a small prediction error of their forward models. Mimicry facilitates communication between two people by giving the forward models an "easy opportunity" to predict actions of the other person. This leads to a small prediction error. A small prediction error in our earlier example of tickling led to a sensory attenuation. However, in the social context instead of a sensory attenuation, a natural reward, namely liking towards the person

is established. A more effective form of communication is established, and better understanding of the person one is interacting with has advantageous effects in evolutionary terms. But also the opposite relationship, in how far liking a person leads to an increase of mimicry, deserves attention. Interacting with a person means the brain is constantly predicting her actions. When liking a person the prediction error made by one's forward models is either small right away and promotes a facilitation of motor responses, which would reveal itself in mimicry. On the other hand the prediction error might be less accurate in beginning and then decrease over time as people become more similar behaviorally over time as well. Mimicry in this sense would then ensure mutual liking, while liking a person from the beginning on does not have an evolutionary advantage (this is not necessarily mutually), a mechanism that would promote mutual liking does have an evolutionary advantage. Mimicry in this sense would then function as a facilitator of social cognition.

Limitations of the predictive coding framework

Andy Clark (2013) concluded that predictive processing models offer the best clue until now for a unified science of mind and action. They promise to unite cognition, perception, action and attention within one framework. This framework suggests a hierarchical, bi-directional processing including top-down and bottom-up connections, where prediction- error minimization functions as the driving mechanism behind many cognitive functions (Clark, 2013).

However, a comprehensive understanding of the physical (i.e. neural) implementation of predictive coding frameworks remains yet to be shown (Egner & Summerfield, 2013). After all what has been illuminated on forward and inverse models within this review came from a computational point of view. According to Marr's (1982) different levels of information-processing, the computational level in itself has to be distinguished from the physical level, thus the implementation of the theory.

A disagreement exists on how this predictive mechanism is implemented. Additionally, it remains to be shown how the predictive and error messages are coded and transmitted via forward and backward connections in a hierarchy (Clark, 2013). Various implementations of the predictive coding theory have been suggested involving different cortical areas and circuits.

Nevertheless, the current lack of a general empirical demonstration of the predictive coding does not restrict its importance on generating theories involving prediction as a likely mechanism of brain functioning. Studies on the neural implementations of predictive coding have been scarce.

DISCUSSION

Summing up the main points, mirror neurons are motor neurons not only firing in response to goal-directed movements but also when the individual is observing or hearing the performance of a similar action. In this sense, mirror neurons are motor neurons used as an internal simulator to understand what another individual is doing

(Gallese & Goldman, 1998). Mimicry is a by-product of this simulation mechanism, which has been shown in higher MEP's recorded from muscles involved in a certain observed action (Fadiga, Fogassi, Pavesi, & Rizzolatti, 1995). By highlighting how mimicry promotes neural synchrony it is emphasized that the opposite direction of this relationship is important as well. However, the MNS approach has often been oversimplified and put in a context in which this approach is used to explain a lot more than what has empirically been shown.

Forward models of motor control rely on a copy of a motor command, established by an inverse model, to calculate an error based on the prediction and the actual feedback from the motor command. A small prediction error leads to sensory attenuation which has evolutionary advantages due to an increased ability to differentiate between self-produced movements and external events. Using the motor system within this review to explain the functioning of forward and inverse models should not overemphasize the relation between forward models and the motor system. After all, a forward model is just a prediction. Seeing it like this, the brain often predicts events without necessarily involving the motor system. Visual perception and automatic processes of the brain, filling in the blind spot for example, are then also a prediction and a kind of forward model.

This functional combination of forward and inverse models has also been applied to social cognition (Wolpert, Doya, & Kawato, 2003). A social interaction loop is established, an interaction between individuals instead of forward and inverse models functioning within one individual. This social interaction loop creates mutual understanding based on predictions by the forward models of each person. Mimicry relates to this by functioning as a facilitator of social cognition. When mimicry is present, a small prediction error is made when predicting motor commands of the other person, which leads to efficient communication, having evolutionary advantages.

Leading back to the beginning of this review, the behavioral consequences of mimicry have been explained to a certain extent. However, what is the underlying mechanism and can neuroscience explain it? Both approaches have their strengths and weaknesses.

The MNS approach relates to mimicry by seeing it as a by-product of simulation. This concept is supported by findings from TMS studies (Fadiga, Fogassi, Pavesi, & Rizzolatti, 1995). The simulation mechanism creates understanding of another person; this leads to liking this person on the one hand and mimicry as a by-product on the other hand. This approach is a reasonable explanation given the current knowledge on the MNS. Nevertheless, the reverse relationship, namely mimicry leading to enhanced liking deserves deeper attention from the MNS viewpoint.

Forward and inverse models of motor control are a well-established concept and based empirical findings. Forward and inverse models have been suggested as a mechanism to explain social cognition (e.g. Wolpert, Doya, & Kawato (2003)). However, linking these theories and findings to mimicry has so far not been approached. The author proposed in this review a possible mechanism, explaining why mimicry leads to enhanced mutual liking, based on forward and inverse models. Mimicry within this approach functions as a facilitator of social cognition, by leading to a small prediction error of the forward model. I think a lot can be

gained when elaborating on this concept in future research. Its usefulness and application has been empirically shown with relation to motor control in humans and future research should aim to apply and proof this model in relation to areas of cognition, however with caution to avoid oversimplification.

When it comes to mirror neurons there has yet to be research, revealing the full functional significance of these cells. Mirror neuron research is still in its infancy and many different approaches using this concept have been elaborated. Forward and inverse models, however, have been an empirically solid proven concept in motor control and are presented as a less speculative concept than the MNS. Findings in relation to the MNS approach have been too vague until now to allow it being a solid independent concept. Especially the hype around mirror neurons in explaining social cognition and causes of autism should be evaluated carefully.

Forward and inverse models on the other hand, are also not the final answer. The concept of internal models can offer a lot to possible mechanisms behind social cognition. But again one could run the risk to oversimplify the topic and apply this approach too easily onto other areas besides motor control. After all, forward models are simply a prediction made by the brain of an individual to estimate future events. So the question arises whether a mechanism behind social cognition must be in the form of a forward model, or whether social cognition has a completely different mechanism behind it. Finally, both approaches reviewed here have been under a lot of investigation, especially mirror neurons. However, at this point in time no clear answer can be given to which mechanism leads to social cognition.

This review summarized findings from the field of cognitive neuroscience and aims to encourage researchers to look at social cognition and especially mimicry from a different angle. Future research should investigate the predictive account of the motor system in relation to social cognition to enlarge the existing concept and to illuminate the link between observed action, the motor system and social cognition (social understanding). Moreover, research focusing on the implementation level of predictive coding approaches is necessary.

Furthermore, many questions remain unanswered with regard to the MNS. For example, it is still unclear why mirror neurons seem to be specific for movements towards objects and food; in case of the macaque monkeys (Fadiga, Fogassi, Pavesi, & Rizzolatti, 1995). Also the exact definition of mirror neurons should be in the focus of research, since many different types of cells, in different functional and structural areas of the brain are now considered mirror neurons. It will most likely happen in the future that meaning and understanding of others will discovered to be not a single process or mechanism, but rather a combination of processes involving motor emulation, abstract cognition and other planning components of the cortex. And we are only beginning to understand their roles.

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JENNY RUTTEN

Jet lag: symptoms, causation and minimization

Review

Jet lag is a misalignment of the human circadian rhythm which is regulated by the suprachiasmatic nucleus in the brain and caused by crossing time zones too fast for the biological clock to keep up. Main symptoms are intense sleepiness or insomnia at inappropriate times. Other symptoms are cognitive impairments, altered digestive functions or depressive symptoms. There is no aid to entirely avoid jet lag, but there are ways to minimize the symptoms, such as phase-advancing or delaying the circadian rhythm before a flight with help of exposure or avoidance of bright light, melatonin and pre-adjusting the sleep schedule. The same resources can be used after arrival to reduce the symptoms. However, many different factors have an influence on the development of jet lag. More research is needed to gain a better understanding of how these are related to each other in detail. The findings are relevant for travelers and traveling workers and shift workers in order to be able to carry out their professional and social activities without the hindrance of jet lag.

Keywords: sleep, jet lag, melatonin, light, biological clock, circadian rhythm

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INTRODUCTION

Jet lag is the set of symptoms that results from a misalignment of the biological clock due to the rapid crossing of time zones to the east or west, shift-work or blindness. These are categorized as 'disorders of entrainment' (Moore, 1997). Entrainment is the process of resetting the internal clock to the external 24-hour rhythm. The human body is used to a certain cycle of light and dark and therefore a certain wake-

and-sleep cycle. This cycle is also known as circadian rhythm: physical, mental and behavioral changes that follow a roughly 24-hour cycle, responding primarily to light and darkness in the environment (Moore, 1997). The name is derived from Latin, where circa means about and diem means day. When this cycle is disrupted suddenly or changed significantly by flying over several time zones, it takes some time for the body to reset this rhythm to the new local time. The resetting of the sleep-and-wake cycle takes a few days and usually brings about some behavioral symptoms. The main symptoms experienced when having jet lag are (intense) sleepiness or sleeplessness at unusual times, depending on whether the flight was westward or eastward (Arendt, 2009; Sack, 2009).

Several questions still arise around jet lag. For instance, it is unclear why certain people do suffer a lot from jet lag while others hardly experience any symptoms. This could be due to individual differences such as age, frequent flying, or the flying circumstances, like direction and number of crossed time zones. Additionally, there is evidence that flying to the west results in few, or even no, jet lag symptoms (Eastman & Burgess, 2009; Haimov & Arendt, 1999; Kalat, 2010; Sack, 2009). However, anecdotal evidence and personal experience suggest that when traveling westward and crossing multiple time zones, there can be quite strong symptoms, like intense daytime drowsiness and waking up very early in the morning, even when going to sleep late.

The answers to these questions and contradictions are beneficial to athletes, aircraft staff, shift-workers and business personnel. If they suffer less from jet lag, they will perform better and suffer less. They could save time by avoiding or minimizing jet lag in advance instead of going a week early to recover from the jet lag on time. The same counts for other passengers who travel through time zones, they do not have to be impaired by jet lag symptoms to perform their daily activities.

This literature review will explain what exactly jet lag is, which factors can alleviate jet lag symptoms and whether jet lag can be avoided. To acquire a better understanding of jet lag and its cause(s), the brain, the biological clock and hormone mechanisms involved in it need to be examined and described. So do the different factors that can contribute to jet lag. Finally, possible approaches for symptoms or jet lag alleviation will be considered. These are medications, staying up until local sleeping time or pre-advancing or -delaying the circadian rhythm and bright light.

METHODS

To address the above mentioned issues and questions, we searched PsycInfo (EBSCO) and started with a broad search term. The first search criterion was “jet lag” and returned 232 hits. To make this search more specific, we changed the criteria to “jet lag” in the “title”, this returned 61 hits. For a general description of jet lag and to find information about the possible treatments, 11 articles were carefully selected. These 11 were selected by reading the titles and selecting those that were not too specific. The remaining articles were not investigated due to limited access (other search networks) or because they were just short reviews. Another search criteria was “jet lag and melatonin”, the useful articles were the same articles as found with

the criteria "jet lag" only in the title. For the more specific matters like jet lag in the elderly and in frequent travelers like air cabin crew, we used Google Scholar and selected articles by the relevant titles.

WHAT IS JET LAG?

When traveling through two or more time zones our biological clock becomes disrupted. Crossing two or less hardly affects individuals (Auger & Morgenthaler, 2009). In this situation we call it jet lag, but the behavioral symptoms related to it also occur in shift-workers. In both cases, the internal clock has to realign to the new circadian rhythm since it is adjusted set to other sleep-and-wake rhythms. It takes some time for the biological clock to reset, hence internal or endogenous signals for sleeping and waking might not match with the local periods of light and darkness (exogenous rhythms). Endogenous rhythms are internally driven (i.e. body temperature), and exogenous rhythms which are driven by an external influence or environmental cue, like light. Usually resetting the rhythm takes about one day for each hour of time zone that is crossed (Haimov & Arendt, 1999).

Typical jet lag symptoms are daytime drowsiness, insomnia and general fatigue. Additionally, depressed mood, cognitive impairment like loss of motivation and concentration, loss of appetite, altered digestive functions, diarrhea and decreased physical performance can occur (Waterhouse et al., 2002) . For most people, the symptoms are worse and they have more difficulties with readjusting when traveling eastward than westward (Arendt, 2009; Srinivasan, Spence, Pandi-Perumal, Trakht, & Cardinali, 2008). Going east, your circadian rhythm gets phase advanced. This means shortening the day, since you fly forward in time. Going west, the circadian rhythm gets phase delayed (Paul et al., 2009). The day becomes longer, because you fly back in time, which is comparable to staying up longer than usual. It is easier to sleep after being awake longer than usual compared to going to sleep earlier before your body's 'sleeping time', because the endogenous period of the body clock is on average a bit longer than 24 hours in the absence of external feedback (Moore, 1997; Schulz & Steimer, 2009). This is also called the free-running period. Taking this into consideration, there seem to be differences in jet lag symptoms after flying eastward or westward. Advancing (after a westward flight) or delaying (after an eastward flight) the circadian rhythm brings about different symptoms. These are intense sleepiness and waking earlier than usual, or, after an eastbound flight, insomnia during local nighttime and drowsiness during the day.

THE BIOLOGICAL CLOCK

The operation of the biological clock starts in the brain, with light entering the eye and causing a cascade of events as shown in figure 1. The results of these events are, amongst others, our circadian, or daily, and circannium rhythms.

Circannium rhythms are our 'seasonal' rhythms. They are more present in animals, for example, they are present for helping birds to know when to fly south before the winter and migrate back north in spring (Kalat, 2010). These rhythms are generated by endogenous pacemakers, the suprachiasmatic nucleus (SCN) in this case. The SCN is located in the brain just above the optic chiasm and lateral to the third ventricle in the anterior hypothalamus. Its primary function is to generate and regulate circadian rhythms. To generate these circadian rhythms, the SCN uses information of light and dark. However, also without that environmental feedback the SCN can generate circadian rhythms (Klein, Moore, & Reppert, 1991).

Circadian rhythms run for approximately 24 hours, usually a little longer than 24 hours in humans (Schulz & Steimer, 2009). Therefore these endogenous rhythms need exogenous feedback to run in 24-hour cycles: a "Zeitgeber", the German word for time provider or determiner. Zeitgeber can be meals and temperature of the environment. At daytime for example, the environmental temperature is higher than at night time. The most important Zeitgeber however, is the light-dark cycle of the day. A recent study suggests that light not only regulates the biological clock, but also cognitive brain functioning (Gaggioni, Maquet, Schmidt, Dijk, & Vandewalle, 2014). To receive this light-dark feedback, a connection between the visual information system and the pacemaker is necessary. The SCN gets this feedback through the retino-hypothalamic pathway. This pathway is the connection from the retina to the SCN and integrates light information with the endogenous cycle, as seen in figure 1 (Isobe & Nishino, 2004; Moore, 1982, 1997). Light perceived through the retina is transmitted through this pathway to the SCN, where the latter controls the pineal gland via the paraventricular nucleus (Isobe & Nishino, 2004). The pineal gland is a small endocrine gland located between the two hemispheres and attached to the third ventricle, posterior to the thalamus (Moore, 1982, 1997). The pineal gland is responsible for melatonin secretion, the 'sleeping hormone'. Melatonin secretion starts a few hours before bedtime. When it becomes dark (evening/night), melatonin is secreted, as light causes suppression of melatonin secretion. This effect is especially pronounced with sun light, although very strong artificial light can cause a similar effect (Lewy, 1983).

Melatonin influences circadian and circannium rhythms. Once those rhythms are set, it is difficult to reset them. After crossing time zones, the inner clock is still set to the 'old' light-dark cycle, thus the endogenous signals do not match with the new exogenous cycle. The inner clock has to reset, this happens slowly. The collection of symptoms caused by this inner clock reset is what we call jet lag (Kalat, 2010; Sack, 2010).

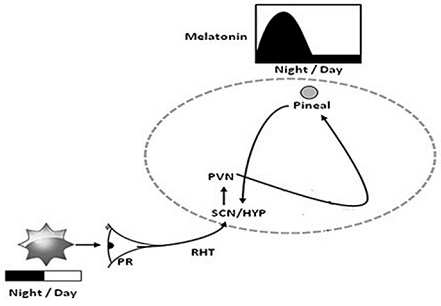

Figure 1: Light is perceived through the retinal photoreceptors (PR) and transmitted through the retino-hypothalamic tract (RHT) to the SCN in the anterior hypothalamus (HYP). The SCN regulates melatonin release from the pineal grand via the paraventricular nucleus (PVN) (Isobe & Nishino, 2004; figure adapted from: http://www.photobiology.info/Tosini.html).

Another factor contributing to the working of our biological clock is the synchronization of circadian rhythm and body temperature. Our body temperature is synchronized to our circadian rhythm, when it is sleeping time the temperature drops. Between 3 and 7 a.m., it is at its lowest. When the core temperature is dropping strongly or when it is at its lowest, it is the easiest to fall asleep. Usually that is at night time, but when jet lagged, the old night time is not the current, so body temperature drops at day time, which makes us sleepy, or it rises at night time, which causes trouble with falling or staying asleep (Waterhouse, Reilly, Atkinson, & Edwards, 2007).

FACTORS INFLUENCING JET LAG

As discussed earlier, when flying westward, we fly back in time. Most likely, sleepiness in the afternoon or early evening and waking up early in the morning will occur, since the 'new morning' is the old noon. When flying eastward, we fly forward in time, which means a few hours of the day are skipped. This results in insomnia at night and waking up late, since one falls asleep later. A study by Lemmer, Kern, Nold, and Lohrer (2002) measured several functions in top athletes after a westbound flight over six time zones (Frankfurt to Atlanta) and an eastbound flight over eight time zones (Munich to Osaka). Several functions including jet lag symptoms were measured. Jet lag symptoms remained until the 5th or 6th day after the westbound flight, and until the 7th day after the eastbound flight. The symptoms after flying east seem to last longer than after flying west, assuming the difference of two time zones is not significant.

The above results do not indicate conclusively that it takes longer to reset the circadian clock after an eastward than after a westward flight, since there is a difference in flight duration and number of crossed time zones (Lemmer et al., 2002). A more plausible explanation for the difference in realignment time is the free-running period of the biological clock. Since we have this natural tendency to prolong our day every day a little bit, it is easier to phase delay the circadian rhythm than to phase advance it (Auger & Morgenthaler, 2009; Eastman & Burgess, 2009; Sack, 2010; Waterhouse et al., 2002). Regarding this data, eastward time zone crossing seems to be harder to recover from due to the more persistent jet lag symptoms and the harder to overcome phase advance, which is likely a result of the free-running period. As the symptoms differ for each direction, different directions might require different treatment strategies.

Nonetheless, travel direction is not the only factor that can contribute to jet lag. Flight duration, how many time zones have been crossed and age of the traveler seem to make a difference in ability to cope with jet lag as well. Flight duration (when flying east- or westward) and number of time zones crossed have similar effects, since increased flight duration (east- or westward) usually results in an increased number of crossed time zones, or the other way around. The severity of jet lag increases when number of crossed time zones increases. Severity here means the symptoms last longer and can be more intense due to the fact that the circadian rhythm needs more time to readjust to bigger time differences. Lemmer et al. (2002) support this. However,

further research should explore whether the difference in more or less severe jet lag experience is due to crossing more time zones or due to different flight directions.

With respect to age effects, Monk, Buysse, Reynolds, and Kupfer (1993) conducted a research where they induced jet lag in elderly people (aged 71 – 91 years) by making them adjust to a 6-hour phase advance. The study was done only with advancing the rhythm, no data was found about a phase delay. They compared the outcomes from participants in their study to the outcomes of younger participants (aged 37-52) from a similar study (Monk, Moline, & Graeber, 1988). The older half seemed to adjust the timing of their circadian temperature rhythm better to the new circadian rhythm than the younger half. On the other hand, the older people seemed to have longer enduring sleep disruption and daytime sleepiness than the younger subjects. In agreement with the latter results, Auger and Morgenthaler (2009) shortly describe a simulated jet lag study. Middle aged subjects (37 – 52 years) and young subjects (18 -25 years) took part in the study. The simulation required a 6-hour phase advance, comparable to an eastward flight where you cross six time zones. The older subjects had more problems with continuous sleeping afterwards, they experienced more interruptions in their sleep and also showed greater impairments in day time alertness. This suggests that with increasing age, there might be more difficulties with coping with jet lag, at least concerning sleepiness. This might be due to the fact that older travelers have more rigid habits and therefore might have more trouble adjusting their biological clock (Eastman & Burgess, 2009; Waterhouse et al., 2002). However, it is rather complicated to draw a conclusion out of the results of the two studies. They are hard to compare because they are about four different age groups between which there might be many differences not controlled for.

Moreover, Waterhouse et al. (2002) found results that make the previous suggestions even more inconclusive. Older subjects suffered less from jet lag and fatigue than the younger subjects who participated in the study. They seem to be more eligible to "pace themselves" than younger people. Cooper (2006) mentions that a few studies and surveys showed that older people might have more trouble with fatigue due to long walks through the airport, stress and carrying luggage than their younger fellows, but that they suffer less from jet lag than younger travelers. Thus, even though it is said that elderly people have more trouble with jet lag symptoms, we cannot draw that conclusion from above mentioned studies since they are quite contradictory.

Special care has to be taken with phase advancing the inner clock, as one has to take a few things into account to not make the advancing work the other way around. One thing for example is if an 'early bird' or a 'night owl', people who are more morning or night active respectively, wants to advance the rhythm. It is harder for a 'night owl' to be inactive early in the night than for an 'early bird'. Moreover, it would be even better for a 'night owl' to delay the phase instead of advancing it, but this also depends on the number of time zones crossed, the desired sleep schedule at the destination and when the person is the most active (morning or evening). The more time zones are going to be crossed, the more beneficial it is for a night owl to delay instead of advance the circadian clock (Eastman & Burgess, 2009).

HOW TO MINIMIZE JET LAG

There are several methods and moments to do something about jet lag. Suggested approaches are bright light treatment, melatonin treatment, pre-adjusting the circadian rhythm, taking departure and arrival times into account or simply 'ignoring' the jet lag and sticking to the local social agenda (Paul et al., 2009). It all comes down to shifting the biological clock as fast as possible to the new time.

Before the flight, circadian rhythms can be advanced or delayed, depending on flight direction. This can be done by going to sleep earlier or later for eastward of westward traveling respectively, in combination with melatonin intake and/or light treatment. The same methods can be used after the arrival, to adjust faster to the local time and light-dark cycles.

When traveling eastward, it is the most helpful to advance the biological clock. This can be done by gradually advancing the time of going to sleep one hour each day and being exposed to bright light straight after waking up. Advancing two hours per day would be too much because it is too fast for the circadian rhythm to adjust (Eastman, Gazda, Burgess, Crowley, & Fogg, 2005). Advancing sleep time can be done by taking melatonin in the evening on the days before the departure (Waterhouse et al., 2007), or increasing the melatonin secretion naturally by staying in dim light. The closer the phase advance before the flight is to the number of time zones to be crossed, the less the circadian clock has to adjust after the flight, and the less one will suffer from jet lag symptoms, hence the less severe will be the jet lag (Eastman et al., 2005). Advancing or delaying the circadian clock before traveling also shifts the moment of the minimum body temperature, which is of big importance when trying to sleep since it helps to initiate and maintain sleep (Eastman & Burgess, 2009).

When traveling westward, the most appropriate approach is delaying the sleeping time combined with bright light exposure in the evening (Sack, 2009). Light is the primary cue for entrainment of the circadian clock, therefore it is of high value to work with bright light when advancing or delaying sleeping schedules (Sack, 2009). This is confirmed by Eastman and Burgess (2009), who describe how melatonin, bright light and sleep schedules can be used to avoid or minimize jet lag. To delay the circadian rhythm before going westward, the best way to do so is exposure to bright light one to two hours before going to sleep and gradually increasing that a few days before the actual flight. Additionally, in combination with the light, going to bed later than usual is of big importance. After waking up, bright light should be avoided. This can be done by sleeping in a dark room, wearing an eye mask when sleeping or wearing sun glasses or something similar when going outside. Nevertheless, even in controlled laboratory studies there are individual differences in how much the phases shift following exposure to bright light (Eastman & Burgess, 2009).

Phase advancing or delaying circadian rhythms before the journey is started, will also shift the moment of the minimum body temperature, which helps initiating and maintaining sleep. Paul et al. (2009) investigated phase delaying and advancing

circadian rhythms with exposure to bright light and the results showed that there were significant phase changes after the treatment. In another study on pre-shifting the circadian rhythm (Eastman et al., 2005), subjects gradually advanced their rhythm with bright light exposure three days before an eastward flight. This showed that advancing circadian rhythms can be used before an eastward flight to reduce jet lag.

To help minimizing jet lag during the flight, sleep should only happen during destination sleep time. It is helpful to use melatonin to facilitate sleeping while being on board (Samuels, 2012). Furthermore, it is important to get as comfortable as possible and to drink plenty of water to avoid dehydration because of the dry cabin air. This can help avoiding or minimizing travel fatigue, but not the actual jet lag symptoms (Haimov & Arendt, 1999). It is important not to confuse the two: jet lag is the result of adaptations that occur when the body has to adjust to a new time zone or a new circadian rhythm. It takes a few days and consists mainly of fatigue, insomnia and impaired concentration. Travel fatigue usually disappears after a good rest and a night of sleep (Waterhouse et al., 2007).

After the flight, it is recommended to adapt the inner rhythm as fast as possible to the external rhythm. Adjusting the biological clock to the local rhythm is easier if the clock is already (partially) phase delayed or advanced, like discussed earlier. Nevertheless, there are some strategies to get rid of jet lag and its symptoms faster with the help of, amongst others, light also when no phase delay or advance has been induced. Since light is the most important time cue for circadian rhythms, it is the primary factor for determining the speed of readjustment to the new circadian clock after arrival (Bear, 2007; Sack, 2009). To adjust faster after an eastward flight, it is helpful to be exposed to bright light immediately after waking up. To adjust the internal time faster to the local time after a westward flight, it is better to be exposed to bright light at 'home' sleeping time.

Regarding taking melatonin, it is questionable whether it would be helpful not only when flying eastward, but also when going west. Since it helps falling asleep, it is most likely only helpful when flying east. That is when insomnia is the most common jet lag symptom and we have to sleep before our body's sleeping time, which is harder than going to sleep after our body's sleeping time, because then we are more tired. When going west, there should not be any problems with falling asleep, but with waking up early in the morning. In that case melatonin will be less helpful, since it mainly facilitates falling asleep and not necessarily maintaining sleep. Taking melatonin at bedtime after an eastward flight is recommended, in contrast to taking it after a westward flight at bedtime. The latter could inhibit phase resetting, while the first could be beneficial for phase resetting. Petrie, Conaglen, Thompson, and Chamberlain (1989) support melatonin as an aid for jet lag with a study where they compared two groups that crossed 8 time zones, one group eastward, the other westward. The people taking melatonin afterwards were significantly faster with realignment and had less jet lag symptoms than the ones who did not take melatonin. Also, melatonin as phase adjuster seems to work better with higher doses, up to 20 mg (Sack, 2009). Other circadian rhythm realignment tools like caffeine do only seem to be helpful to increase alertness. Meals at the appropriate times and social agenda seem to enhance circadian adaptation as well, as they work as 'Zeitgeber' or exogenous rhythms (Samuels, 2012).

With regard to timing of flying, Waterhouse et al. (2002) conducted a study where they observed a sports team during its flight from the United Kingdom to Australia. The whole journey would take about 24 hours. One of the independent variables was arrival time in Australia. One flight left in the morning (arriving in Australia in the afternoon, local time), group 1, and the other in the evening (arriving early in the morning at local time), group 2. The morning departure would go to sleep at night after being up for 30-35 hours and the evening departure after being up for 50-55 hours. Regarding this information, one would suggest that the morning group (1) would suffer less from fatigue than the other group (2). The results showed that the group that would arrive in the morning, group 2, slept significantly more during the flight. The group that arrived later in the day, group 1, had fewer problems with jet lag effects. Another finding was that the people on the evening flight, group 2, suffered more from fatigue in the noon and afternoon than the other group did. The phase disruption is less for the morning departure group 1. They lost less hours of sleep than the second group because the time period between the last and next full sleep is shorter. So arriving later on the day after an eastward flight is more beneficial for the traveler than arriving early(Waterhouse et al., 2002). It also seems to be beneficial to choose daytime flight as such that it minimizes sleep loss. Additionally to eventually take some melatonin or hypnotics to induce some sleep at night flights to minimize the fatigue and loss of sleep (Haimov & Arendt, 1999).

Summarized, the best way to avoid or minimize jet lag is to phase advance or delay the circadian rhythm as close as possible to the destination time rhythm a few days before the journey starts. Depending on direction and flight duration, the most beneficial sleep, departure and arrival times can be variable.

JET LAG AND FREQUENT TRAVELING

When flying frequently and crossing many time zones east and west, it can be very exhausting to adjust from one circadian rhythm to the other. How do shift workers, aircraft cabin crew, and other frequent flyers deal with this, especially since such travelers (or employees) suffer often or chronically from jet lag (Sack, 2009)?

In a study by Waterhouse et al. (2002), jet lag effects were measured in athletes after eastward flights from the United Kingdom to Australia. The results showed that the athletes who traveled the same journey before experienced the jet lag worse than the subjects that had not made the journey before. Also, the subjects that had traveled to Australia before showed more fatigue at noon and in the afternoon than the subjects for who this trip was the first time. This might have been due to the fact that they were more impressed and occupied by the new experiences and did not know what to expect and therefore probably paid less attention to the symptoms, as opposed to the subjects that had done the journey previously (Waterhouse et al., 2002).

Due to the few and limited studies or methods on how pilots and other frequent travelers deal with the regular jet lag troubling, we can only suggest how they recover or deal with the recurrent jet lags. The most convenient approach, especially for short duration trips, would be to maintain the same sleep schedule like at home. With this

approach, the circadian rhythm would not change, which means that it does not have to realign and consequently no realignment symptoms (jet lag) would occur. If travelers do this, they sleep better and longer and have less jet lag effects. The only problem with this approach would be the social activities at the local destination, which they might not be able to attend because they are sleeping at home times. If the trips are of longer duration, it is important to adjust as fast as possible to the new circadian alignment, which can be done by earlier mentioned methods (Sack, 2009). A study done by Petrie, Dawson, Thompson, and Brook (1993) showed that taking melatonin may have benefits for cabin crew for a faster recovery from jet lag.

If the cause of jet lag is understood and when it can be counteracted, some health issues can be resolved in advance, as frequent jet travel and regularly being jet lagged has some health implications. Some of them are cognitive deficits, temporal lobe atrophy and menstrual cycle disturbances (Eastman & Burgess, 2009). Also, meals will be eaten at inappropriate circadian phase moments and repeated occurrence of this can cause weight gain which in turn can increase the risk of getting diabetes and cardiovascular problems. In short, frequent traveling is not beneficial for health and depending on the duration of the trip, it can be better to maintain the home sleep scheduled (Eastman & Burgess, 2009).

DISCUSSION

The primary aim of this review was to describe jet lag and its determinants and what can be done about it. The misalignment, the process of realignment and the symptoms after crossing time zones too fast for the biological clock to keep up, are collectively referred to as 'jet lag'. It turns out that many factors contribute to jet lag and its severity. As mentioned earlier, one of the contributing factors is flight direction. Flying eastward brings about more severe and persistent symptoms than flying westward (Auger & Morgenthaler, 2009; Haimov & Arendt, 1999; Kalat, 2010). Lemmer et al. (2002) show that athletes who flew eastward needed more time to adjust to the new rhythm than the athletes who flew westward. However, the eastward flight crossed two more time zones than the westward flight. Hence, all we can conclude from this study is that the crossing of more time zones brings about more persistent symptoms. Additional studies should investigate this effect with comparing east- and westward flights of equal time length. Perhaps return flights are suited for this kind of research. Both between-subject and within-subject effects can be explored this way.

Another factor which is said to influence the ability to cope with jet lag is age. However, there is disagreement about this. It is suggested that elderly people have more severe and longer lasting jet lag symptoms than younger people (Cooper, 2006; Waterhouse et al., 2002). Whether or not this is the case, still needs to be investigated. Studies that have confirmed these findings are simulations of phase shifting (Auger & Morgenthaler, 2009; Monk et al., 1993). The participants never crossed time zones and did not experience the social agenda after arrival because the study took place in an isolated and adjusted environment. Moreover, one study suggests that older people seem to be better in adjusting their circadian temperature

to the new circadian rhythm than younger people (Monk et al., 1993). Besides these contradictive findings, there might be a problem in the definition of jet lag in the mentioned studies. The actual definition (symptoms of a misalignment of the circadian rhythm to the new local time) might be mistaken for general travel fatigue. Another limitation is that there are only studies done on phase advancing simulation and not on phase delaying. Future studies should take these limitations into account by using data of elderly flight passengers when 'naturally' crossing times zones instead of simulating time zone crossing. This is also more cost-efficient.

Another question in this review was whether it is possible to avoid or minimize jet lag symptoms. The literature only suggests ways to minimize symptoms and not to avoid them. The most efficient way to do so is to phase-advance or -delay the inner clock for respectively east- or westward crossing of time zones. The more the biological clock is adjusted prior to the journey, the easier it is to realign to 'the rest' of the rhythm. Even though these are the most effective methods, they have to be done with care. The delaying or advancing has to be done gradually; if the 'manual' phase shifting is done too fast, the inner circadian clock will not be able to keep up and jet lag symptoms will be experienced even before the actual flight (Eastman et al., 2005). However, even though phase shifting the circadian rhythm is more beneficial than only trying to minimize the symptoms after an abrupt time zone transition, it is not effortless. One has to make an effort to actually carry out the rhythm pre-adjustment. The largest sacrifice of advancing or delaying the sleeping schedule though, might be the missing out on social events and activities (Eastman et al., 2005).

To realign the inner and outer circadian rhythms after the flight, it is helpful to give the inner clock exogenous 'Zeitgebers' as realignment guide. These can be meals or social agenda for example. More important however is exposure or avoidance of bright light and taking melatonin at appropriate times. Although this can be troublesome if there is no access to bright light due to weather circumstances or an activity schedule. Also, the effect of light seems to vary with age, psychiatric status and changes in sleep homeostasis (Gaggioni et al., 2014).

Last but not least, the effect of frequent traveling on jet lag was explored. One would expect it causes habituation and consequently more ease to deal with, however, the opposite seems to be the case in the only study found on this issue. Athletes that traveled frequently suffered more from jet lag symptoms than athletes new to traveling (Waterhouse et al., 2002). This suggests that frequent time zone crossing rather brings awareness of jet lag symptoms instead of habituation or tolerance. However, if one travels often through time zones, it will be easier to learn how to adjust as fast as possible to the new circadian cycle. It should be clear that further research on the relation between jet lag and frequent traveling is necessary to elucidate the effects.

As known for now, jet lag severity is most dependent on the circumstances on the flight rather than personal differences, as there is limited evidence for the latter. Flight direction can make a difference, and so do flight duration and amount of time zones are crossed. Jet lag from flying eastward seems harder to overcome than after flying westward and it makes a big difference when one adjusts his or her circadian home rhythm to the rhythm of the destination. The current methods to minimize jet lag symptoms seem to work, although they are not without effort.

This literature research has thrown up many questions in need of further

investigation. Now that we know that there are methods to minimize jet lag, it becomes interesting to think about the possibility to ever become resistant for circadian shifting. It is of special interest for shift workers, athletes and air craft crew, even more than knowing how to suffer as little as possible from jet lag. Hence, maybe this could be the next step in research about how to cope with jet lag, shift work and traveling through time zones. Furthermore, one could think about establishing the effects of personal differences such as the difference between 'night-owls' and 'morning-birds' in their relationship to jet lag. It is known that the two benefit from different strategies concerning phase-advancing and delaying, but specific studies are necessary to elucidate the exact relationship. Another future direction is age; many contradicting effects can be sorted out by studying the effect of time-zone crossing in higher age travelers instead of simulating in an unnatural environment. As a final suggestion for future work, the effects of light on cognitive functioning and the differences in effectiveness of light with regard to age, morning or evening person and psychiatric status should be explored in detail.

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DANIËLLE STARREVELD

The Need for Psychosocial Interventions in Oncology Care

ESSAY

In a recent report, the Dutch College of Health Insurances (College van Zorgverzekeringen, CVZ) proposed to remove the costs for psychosocial interventions in oncology care from the basic health insurance repayments. The current essay argues that psychosocial interventions are a valuable addition to the biological treatment of cancer patients. The prevalence of psychosocial problems in cancer patients might be similar to the prevalence in the general population. Psychosocial interventions to treat these problems can be divided in five groups: provision of information, group therapy, training in coping skills, psychotherapy and spiritual/existential therapy. Studies on the effectiveness of these interventions show contradicting results that can be explained by lack of screening for psychosocial problems during recruitment and methodological issues. Furthermore, following the trend in medical cancer treatment, psychological treatment should be more individualized. It is therefore suggested that the CVZ should keep covering these costs in their basic health insurance.
Keywords: Cancer, Quality of Life, Psychological Well-being, Psycho-oncology, Prevalence

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INTRODUCTION

Due to early detection and the improved (palliative) care the number of patients with a diagnosis of cancer has increased (Meulepas and Kiemeney, 2011). This development leads to more attention to the psychological consequences of the

illness, reflected in the development of psycho-oncology units in cancer centres since the 1980s, increased behavioural research, and the public education in cancer prevention in the 1990s (Breitbart & Alici, 2009). According to Breitbart and Alici (2009), fifty per cent of cancer patients experience psychiatric disorders related to their cancer diagnosis

According to Holland and Gooen-Piels (2000), the general reaction to a diagnosis of cancer can be described in three phases. In the first phase, called the *initial phase*, patients show symptoms like disbelief, denial or despair. The diagnosis creates a period of crisis that makes it hard to process the important information that is given to a patient during this phase. This phase usually lasts less than a week. The second phase is called *dysphoria*. Dysphoria and emotional turmoil are typical in this phase where patients slowly start to acknowledge their diagnosis of cancer. The thought of the disease intrudes repeatedly and it cannot be banned. Symptoms like anxiety, depression, poor concentration, and insomnia are often seen. Dysphoria usually lasts one to two weeks and diminishes when a treatment starts. The last phase of a general reaction to a diagnosis of cancer is *adaptation*. In this phase, a patient resumes to normal activities and accepts the diagnosis. Patients find reasons to be optimistic. This phase lasts for months and ends with a transition to normal life. The quality of adaption depends on the coping style of a patient, which is formed by previous crisis experiences of a patient. This results in individual differences in the most optimal coping style and indicates that the most optimal coping style for all patients with cancer does not exist. A good coping style results in an adjustment to the diagnosis.

It is this adjustment that creates variety in the response to a diagnosis of cancer between individuals. Different factors influence this adjustment, which can be divided in three factors: society-derived, patient-derived and cancer-derived (Holland & Gooen-Piels, 2000). The *society-derived* variables describe the attitude of a society towards cancer and the treatment. *Patient-derived* variables have three sources: an intrapersonal source determined by the developmental stage and the coping style of a patient, an interpersonal source represented by the social environment of the patient and the socioeconomic and social class of an individual. The final factor that influences the adjustment to the diagnosis cancer is *cancer-derived variables*. The clinical aspects of the disease and the psychological support of nurses and doctors are part of these variables (Holland & Gooen-Piels, 2000).

Due to the increasing numbers of patients with cancer, more patients are affected by the long-term physical and psychological consequences of the illness (Meulepas and Kiemeney, 2011). Despite these increasing numbers the Dutch College of Health Insurances (College van Zorgverzekeringen; CVZ) suggested removing the repayment of the costs for these interventions from the basic health insurance in the Netherlands (van Diggelen & Kroes, 2013). The CVZ suggested that psychological care is integrated in the biological treatment of cancer. Another suggestion is that the best treatment for patients with an adjustment disorder is removing the stress factor, in this case the cancer.

The question arises whether the CVZ is right to propose removing the costs for these interventions from the basic health insurance, or whether these interventions are in fact effective and should be available as basic health care. Therefore, the

present review describes first the prevalence of psychological problems in cancer patients. Second, the available psychological interventions, and finally discusses the effectiveness of these interventions.

PREVALENCE OF PSYCHOSOCIAL PROBLEMS IN CANCER PATIENTS

Most studies about psychiatric disorders report the prevalence of depression, anxiety disorders, and psychological distress in oncology patients (Aass, Fosså, Dahl, & Moe, 1997; Minagawa, Uchitomi, Yamawaki, & Ishitani, 1996; Okamura, Yamawaki, Akechi, Taniguchi, & Uchitomi, 2005). According to Derogatis et al. (1983), the prevalence of psychiatric disorders in cancer patients is 47%. This prevalence is three times as high as the prevalence of psychiatric disorders in the general population. However, Van't Spijker, Trijsburg, and Duivenvoorden (1997) performed a meta-analytical review of 58 studies after 1980 and found much smaller differences between cancer patients and the general population. Their results described a prevalence of depression disorders in up to 46% for cancer patients. A comparison with the general population resulted in a d-value of 0.20, which indicates a small difference between the prevalence of depression in both populations. A prevalence of 1 to 49% is reported for anxiety disorders. Psychological distress is measured by 5 to 50% of the cancer patients. Both prevalence ratings did not differ from the prevalence of anxiety disorders and psychological distress in the general population. Van't Spijker et al. (1997) suggested that these findings were more robust because they compared different studies where Derogatis et al. (1983) only described one study.

Furthermore, van't Spijker et al. (1997) described that the prevalence of depression in oncology patients does not significantly differ from the general population when only the studies after 1987 were considered. Van't Spijker et al. (1997) explain this finding as a consequence of an attitude change towards cancer since the 1980's. Patients were better informed and the medical treatment for cancer was improving. The diagnosis of cancer is at an earlier stage and therefore the average patient's age at the moment of diagnosis is lower than before the 1980's. Early detection in turn resulted in better prognoses, which lead to less psychosocial problems. Therefore, it is suggested that the prevalence of psychosocial problems in oncology patients is comparable with the general population in recent times. In a more recent study completed by Kadan-Lottick, Vanderwerker, Block, Zhang, and Prigerson (2005), 251 advanced cancer patients were recruited. The prevalence of psychiatric disorders was determined through questionnaires on major depressive disorder, generalized anxiety disorder, panic disorder and post-traumatic stress disorder. The prevalence of these psychiatric disorders was not significantly different from the general population, confirming afore-mentioned results.

There are thus conflicting conclusions regarding a higher prevalence of psychosocial problems in patients with cancer (Derogatis et al., 1983) versus no differences in prevalence (Kadan-Lottick et al., 2005; van't Spijker et al. 1997). However, it should be taken into account that methodological issues (i.e. the use of two different questionnaires to determine depression) could explain the conflicting

numbers on the prevalence of psychosocial problems (Ciaramella & Poli, 2001). Other factors that could lead to conflicting results are the used definitions of depression, the time since the diagnosis of cancer, history with depression and treatment for cancer (Newport & Nemeroff, 1998). It thus remains unclear whether or not the prevalence of psychosocial problems in cancer patients is heightened compared to the general population. The CVZ based its opinion that oncology patients should not be treated differently from the general population on the studies of Kadan-Lottick et al. (2005) and van't Spijker et al. (1997). Future research is necessary to shed light on the true prevalence.

PSYCHOLOGICAL INTERVENTIONS FOR CANCER PATIENTS

A variety of psychological help is available for patients with cancer. Examples are psycho-education, cognitive behavioural therapy, client-centred and experiential psychotherapy, psychotherapy, systemic family therapy, group therapy and music therapy (de Haes, Gualthérie van Weezel, & Sanderman, 2009; Hart, 2009). The hierarchy of psychological interventions by Cunningham (1995) describes different forms of available therapy (see Fig. 1). The bottom of this hierarchy should be available for every patient. The top of this hierarchy consists of intensive therapy for patients who need elaborate mental health care.

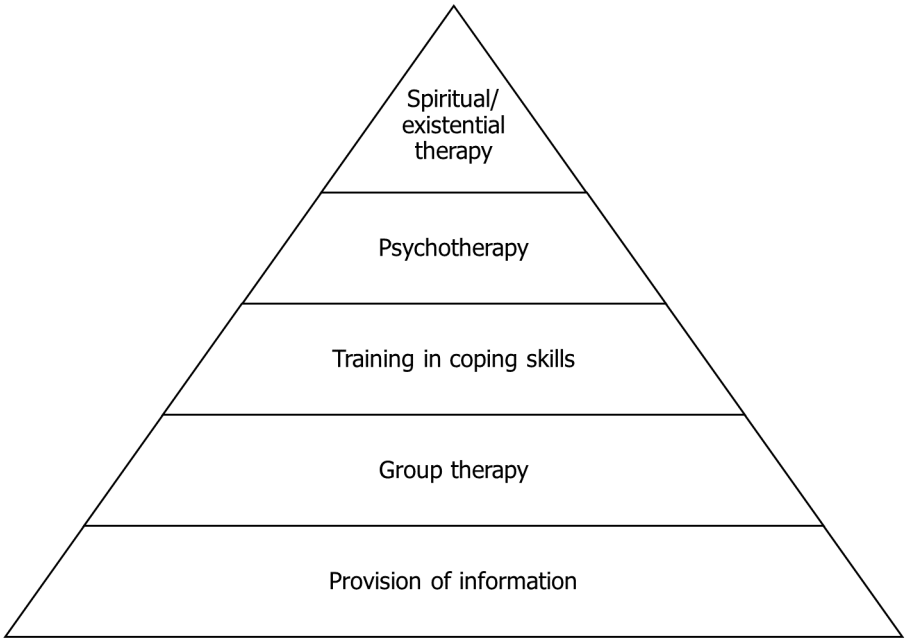

Figure 1: The hierarchy of psychological interventions of Cunningham (1995).

Provision of information

Provision of information is at the bottom of the hierarchy proposed by Cunningham (1995). This type of psychological care focuses on providing information for cancer patients. An example is psycho-education. According to Gualthérie van Weezel and de Jong (2009) the provision of information helps patients adjust to their new situation. Health care providers explain which difficulties cancer can cause and how to deal with these difficulties. This intervention is a direct effect of the development of psycho-oncology in 1980's. Since the 1980's, more attention was given to the patient and his or her involvement in the treatment. A patient needed to be informed about the diagnoses of the disease to make a decision about treatment. This is thought to lead to a heightened feeling of control over the situation, which could help patients cope with their illness.

Group therapy

One level higher on the hierarchy is group therapy. This form of therapy aims to assist individuals in admitting the effects of the disease and to show their emotions to the individuals around them (Cunningham, 1995). Patients come together to talk with each other. The idea behind this intervention is that individuals live and learn in groups during their lives. When an individual receives the diagnosis cancer the patient can have the experience that he or she is alone. The group experience returns when these individuals talk with other individuals that are going through the same process. Patients remember that they are not alone (Pet, de Ruiter, & Barkmeijer, 2009). Effects of group therapy are an improvement of the psychological wellbeing and decrease of depressive and anxiety symptoms. Altogether this leads to an increase of quality of life, better coping and mental adjustment to the disease (Weis, 2003).

Training in coping skills

Provision of information and group therapy should be available to the majority of the cancer patients, whether they experience psychosocial problems or not (Cunningham, 1995). However, training in coping skills is a more intensive therapy suited for patients who developed some form of psychosocial problems after a diagnosis of cancer. This type of therapy is less frequently used and placed on the third level of the hierarchy of Cunningham (1995). An example of this type of intervention is cognitive behavioural therapy (CBT). The aim of CBT is to develop new cognitive skills that help patients to adjust better to the disease.

CBT in oncology care is based on the idea that the personal meaning of the disease determines how a patients copes with the disease. As noted before, every patient has his or her own coping style to adjust to the diagnosis cancer. When a patient does not adjust well to the diagnosis of cancer emotional and behavioural problems arise. This is caused by wrong associations that patients have about cancer. An example of a wrong association is: "I have cancer, nothing can be done to save me." In CBT, patients identify existing associations, thoughts causing these associations and inspect whether or not these thoughts are correct together with

a therapist. The incorrect thoughts are rectified (Schroevers, van der Lee, & Pet, 2009).

Psychotherapy

Cunningham (1995) places psychotherapy on the second level of psychological care for patients with cancer. Psychotherapy is based on psychoanalytical grounds. It assumes that in the human psyche conscious and unconscious processes work together. The unconscious processes influence the behaviour of an individual. Examples of unconscious processes are defence mechanisms that help to protect an individual from situations that are too threatening to handle. A diagnosis of cancer is an increased threat to life, which most patients can process themselves. Yet, some patients need extra help to cope with this increased threat and psychotherapy can be a solution. During this therapy the patient and the therapist build a confidential relationship. Together they will work out which defence mechanisms are used by the patient and where they come from. With the knowledge of these repressed thoughts, the therapist and patient work to adjust the defence mechanism to cope with the life threatening disease (van Schoonheten, Gualthérie van Weezel, & Ploegmakers-Burg, 2009).

Spiritual/existential therapy

The top of the hierarchy for psychological interventions describes spiritual/existential therapy (Cunningham, 1995). The basic idea behind this therapy is that an individual puts all attention to the here and now and tries to identify the physical and emotional feeling related to the illness. It gives patients the opportunity to determine the current emotions elicited by the diagnosis of cancer while ignoring emotions from the past or emotions that are expected by others. The aim of the therapy is to label current emotions and deal with them. The therapist leads a patient in this process (Vedder & Maas, 2009).

The hierarchy of psychological interventions of Cunningham (1995) suggests that there is a fitting psychosocial intervention for every patient with cancer. It also suggests that most patients do not need specialised mental health care as long as they receive valid and understandable information. Other patients need more assistance to adjust to the illness. Yet, the question remains whether or not these interventions really improve the adjustment to the diagnosis of cancer.

EFFECTIVENESS OF PSYCHOSOCIAL INTERVENTIONS

Meyer and Mark (1995) reviewed several studies on psychosocial interventions in oncology care and concluded that psychosocial interventions have a positive effect on cancer patients. It improves the emotional and functional adjustment and symptoms related to the illness and medical treatments are decreased. However, some studies described no effect or a small effect, whereas others described large

effects. There are several explanations for these contradicting findings. First, inclusion criteria differ between studies. None or limited inclusion criteria resulted in a high heterogeneous group of participants of which some already adjusted to the disease. Psychosocial interventions will have a small effect on these patients and distort the effect size of the intervention seen in patients who are in need for psychosocial care (see fig. 2). Second, some interventions have a small effect, do not work, or only work in a small group of patients that makes it difficult to detect an effect (Ross, Boesen, Dalton, and Johansen, 2002). Third, a comparison of different single intervention studies leads to a comparison of heterogeneous variables (i.e. measurement type and participants) and differences in methodology (i.e. the use of a control condition and randomization).

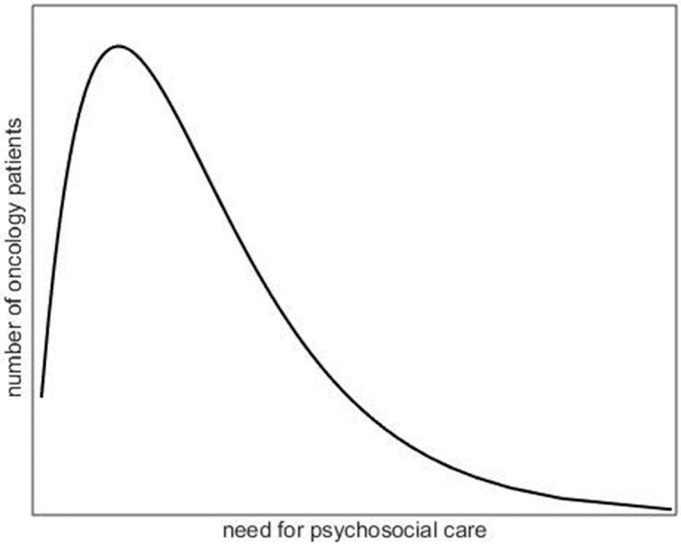

Figure 2: Distribution of the number of oncology patients and their need for psychosocial interventions. Most patients with cancer are on the left side of this distribution, representing no or a low need for psychosocial interventions corresponding to the lowest level of the hierarchy by Cunningham (1995). Few patients are on the right side of the distribution, representing that they need psychosocial interventions and could benefit from psychosocial intervention on the higher levels of the hierarchy by Cunningham (1995).

Rehse and Pukrop (2003) addressed the third problem in a meta-analysis on the effectiveness of psychosocial interventions for patients with cancer. A measurement of quality of life (QoL) was constructed to reduce the problem of heterogeneous variables from different studies. Results indicated that psychosocial interventions have a positive effect on QoL in adult patients with cancer. Based on these results, Rehse and Pukrop (2003) suggested that psychosocial interventions should be part of the standard care for cancer patients, which is in line with the proposal of Cunningham (1995). The costs of implementation are low in comparison with the high benefit of a better quality of life for cancer patients. However, more research is needed to tailor psychological treatment to the individual patient's needs.

According to Tamagawa, Garland, Vaska, and Carlson (2012), there is not a single, most optimal psychological intervention for every patient with cancer. It is suggested that psychosocial characteristics of an individual are moderators for the effect of a psychosocial intervention. These moderators can be divided in four categories. The first category is *personality traits*, i.e. optimism. Individuals who score low on optimism benefit more from psychosocial interventions in comparison with individuals who score high on optimism. The second category is *mental and psychical quality of life*. Patients who experience physical limitations before the start of their treatment experience more benefits from the intervention compared to patients who do not experience physical limitations. *Social support* is the third category. When a patient experienced less social support than the psychosocial interventions had more effect. The final category is *self-efficacy*. The moderating effect of this category is two-sided. Individuals with low-levels of self-efficacy benefit from interventions, but high levels also benefit from some interventions (Tamagawa et al., 2012).

The author believes that many studies suffered from severe methodological challenges. Screening for psychosocial problems of patients with cancer would yield encouraging effectiveness results in future studies. A recent study by Rykov (2008) is an example that showed that screening can have positive effects on the reported effect size of psychosocial interventions. Rykov (2008) summarized experiences of a group-based music therapy for patients with cancer who were not diagnosed with psychosocial problems or reported them to a physician. Based on personal stories, Rykov (2008) concluded that this type of therapy is empowering and provides the oppurtunity to experience a feeling of control that was lost since a diagnosis of cancer. The sample of this study was self-selected, reflecting patients on the right side of the distribution of oncology patients and their need for psychosocial interventions (fig. 2). The results showed that psychosocial interventions can have positive effects in patients who wanted more help to cope with their diagnosis. This interest plays an important positive role in the effect of an intervention (Carlson & Bultz, 2008). No interest in an intervention might result in opposite effects, such as more distress (de Moor et al., 2002).

DISCUSSION

Research about the prevalence of psychosocial problems and the effectiveness of psychosocial interventions in oncology patients led to contrasting results. These contrasting results are also seen in studies about medical treatments for cancer. When clinical trials in oncology care are compared to clinical trials for other diseases, results indicated significant differences in oncology research. The life-threatening aspect of cancer and quick development of innovative treatments make it easier to start with early-phase trials. However, most of these studies have small sample sizes and no control conditions leading to heterogeneous results, the absence of clear answers and no knowledge on the long-term side effects of medical treatments of cancer (Hirsch et al., 2013).

According to Bernards (2013), the term cancer does not describe a disease that is equal for every patient. It might seem that every form of lung cancer is the same, but this is not the case. Every patient is different because cancer is caused by an individually unique mutation in the DNA. Therefore the medical treatment of cancer has to be individualized. An example of this is the treatment of a melanoma. Patients with a specific genetic mutation receive a specific kind of medication that gives them a better chance on survival. In the near future it should be possible to treat most forms of cancer according to this mechanism: an individual combination of medication based on the DNA of the patient.

Recent developments in the medical treatment of oncology acknowledge the fact that every person is unique. The fact that every patient is unique also needs to be acknowledged in the psychosocial care for cancer patients. There are patients who receive a diagnosis of cancer and develop psychosocial problems because of it (van't Spijker et al. 1997). In order to prevent that these problems get unbearable for patients, screening these problems is necessary. In this way patients at risk are detected at an early stage and effective interventions can be offered immediately.

Another question remains whether these psychosocial interventions should be available for all patients with cancer. One could vote in favour of this statement because every patient goes through a general reaction process to a diagnosis of cancer (Holland and Gooen-Piels, 2000). However, a recent study by Rykov (2008) indicated that a group-based music therapy had very positive effects in a self-selected sample of patients with cancer. Moreover, de Moor et al. (2002) indicated that offering a psychosocial intervention to patients who are not interested in it has detrimental effects. These unfavourable effects would plead to offer psychosocial interventions only to the patients who are in need of it.

The CVZ proposed to remove the costs for psychosocial interventions in cancer treatment from basic health insurance. This proposal could be defended by the indication that the prevalence of psychosocial problems in patients with cancer is similar to the prevalence of psychosocial problems in the general population (van't Spijker et al., 1997). Following this reasoning it seems clear that psychosocial interventions are not important in cancer care and that these costs could be cut from the basic health insurance. Furthermore, it is not clear whether or not these interventions are effective (Ross et al., 2002). Yet, it is important to note that small effects might disappear in meta-analyses and that it is likely that not every patient would benefit from a psychosocial intervention (Tamagawa et al., 2012) This is a critical factor that may well have distorted reviews about the effectiveness of psychosocial interventions (Meyer & Mark, 1995; Ross et al., 2002).

Even though the scientific research is not conclusive about the beneficial effects from psychosocial interventions, it should not be forgotten that there are patients in need of psychosocial care. Until it is not clear who benefits from these interventions and who does not, psychosocial interventions should be available for those who search for it. Rykov (2008) showed that psychological interventions are very effective in patients who ask for them. But when the costs of these psychological interventions are removed from the repayment list of the basic health insurance,

these individuals might not be able to use them. Less patients participating in interventions means less research on the subject. And that means that the real effect and the real importance of these interventions will stay unknown.

So, the prevalence of psychosocial problems in patients with cancer might be similar to the prevalence of psychosocial problems in the general population. Moreover, contradicting results do not offer clarity on the effectiveness of psychosocial interventions for every cancer patient. Even though these uncertainties exist, the CVZ should offer a repayment for psychosocial interventions in oncology care from the basic health insurance. The effects of these interventions can be priceless for the patients who need them. Insurance companies should not deny this form of help to patients that are experiencing a difficult and uncertain time in their life and are asking for help in coping with cancer.

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RIK UBAGHS

Abnormal Volumetric Alterations in the Schizophrenic Brain

Original Paper

Different lines of evidence support a role for the cerebellum and the hippocampus in the pathology of schizophrenia. The involvement of the cerebellum might be represented in structural deficiencies in patients with schizophrenia. The current research investigates the possibility of volumetric differences between healthy controls and patients suffering from schizophrenia.

Volumetric measures were obtained from nineteen patients diagnosed with first episode psychosis, early psychosis or established schizophrenia and thirty healthy controls using a 1.5 Tesla magnetic resonance scanner. Results show a significant difference in the association patterns between groups in the structures of interest. This indicates possible structural abnormalities in the hippocampus and cerebellum, associated with the pathology of schizophrenia.

Keywords: Schizophrenia; MRI; Volumetrics; Hippocampus; Cerebellum

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INTRODUCTION

Schizophrenia is a disorder that affects 1 - 2% of the population, and globally accounts for 1.1% of the disability adjusted life years. Because of this high level of incapacitating effect, schizophrenia is one of the most expensive pathologies in modern day health care (Picchioni & Murray, 2007). In recent years, schizophrenia has been conceptualized as a disorder caused by neurodevelopmental deficits (Insel, 2010), and neuroanatomical research has focused mainly on the higher cortical areas. Although schizophrenia is best known as a disease of cognition (Keefe, Eesley, & Poe, 2005) with no apparent pathology in motor function, the majority of patients (50-65%) show a variety of motor impairments (Bombin, Arango, & Buchanan, 2005;

Heinrichs & Buchanan, 1988). Recently it has been proposed that these deficits in motor coordination, combined with cognitive symptoms such as disinhibition and sensory integration, could imply a possible involvement of the cerebellum in the pathology of schizophrenia (Andreasen et al., 1996; Thomann et al., 2009).

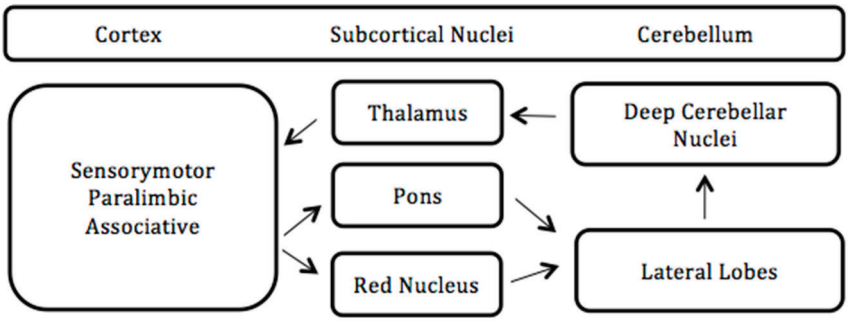

Figure 1. Sensorimotor and high-order information is carried from the cerebral cortex to the pons, after which fibbers carry the projections to the lateral lobes of the cerebellum. Additional projections from the cerebral cortex run through the red nucleus, where they synapse and subsequently give rise to the central tegmental tract that runs to the lateral cerebellar lobes. The deeper nuclei of the cerebellum project back to the cortex and close the loop (Andreasen et al., 1996).

Traditionally, the cerebellar structure is thought to be involved mainly in motor functioning, conditioning and coordination (Mottolese et al., 2013). Conversely, the use of modern paradigms combined with diffusion tensor imaging (DTI) tract-tracing methodologies, has lead researchers to believe that the cerebellum is also involved in higher cognitive functioning through multiple neural pathways involving subcortical structures such as the pons and the thalamus (Thach, 2007). Through these circuits, the cerebellum is able to project to sensorimotor, autonomic and multiple association cortices (Allen et al., 2005; Jissendi, Baudry, & Baleriaux, 2008).

One of the most evident pathways, the cortico-cerebellar-thalamic-cortical (CCTC) circuit, allows the higher order association areas to transfer information to the cerebellum through the basilar pons (Fig. 1). After processing the signal, the dentate nucleus of the cerebellum sends the information back to the frontal cortex and other related cerebral areas, making bidirectional information streaming possible (Andreasen et al., 1996; Middleton & Strick, 1994; Schmahmann & Pandya, 1997). These circuits are believed to allow the cerebellum to be involved in higher cognitive functions including reasoning and executive planning. Andreasen and Pierson (2008) proposed that the cerebellum operates as a regulatory mechanism within the CCTC circuit. During normal functioning, Purkinje cells decipher information that arrives at the cerebellum, and as a consequence, the input programs the cerebellar Purkinje cells by means of long-term depression. This programming allows the cerebellum to detect variations in the input signal and modulate the information in an inhibitory manner. Conversely, schizophrenic patients show symptoms

of cognitive dysmetria, which include difficulties in the coordination of mental processes. This disability could derive from a failing of the cerebellum to connect the information in the right order due to structural abnormalities. The information, directly relayed to the cortex, is then presented in a desynchronized manner, and the patient experiences a slowing of cognition (Andreasen & Pierson, 2008). The slowing of cognition combined with the wrong order of the input to the higher areas of the cortex could lead to symptoms relatively common in schizophrenia, including blurred thought and impaired speech, as well as hallucinations and loss of volition (Andreasen et al., 1999; Andreasen & Pierson, 2008; Mouchet-Mages et al., 2011).

Modern imaging techniques provide further evidence supporting the involvement of the cerebellum in schizophrenia (Crespo-Facorro et al., 2001; Paradiso et al., 2003). For example, functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) studies have shown a decreased blood flow in patients' cerebellum and other brain areas in response to tasks involving recognition memory and attention (Andreasen & Pierson, 2008; Crespo-Facorro et al., 1999). Structural volumetric studies have also shown abnormalities in cerebellar matter in schizophrenia. Using imaging modalities such as computed tomography (CT) (Heath, Franklin, & Shraberg, 1979; Weinberger, Torrey, & Wyatt, 1979) and magnetic resonance imaging (MRI) (Ichimiya, Okubo, Suhara, & Sudo, 2001; Loeber, Cintron, & Yurgelun-Todd, 2001; Okugawa, Nobuhara, Takase, & Kinoshita, 2007), research suggests that cerebellar matter was reduced in schizophrenic patients as compared to healthy controls. MRI studies have shown a particular reduction in the right vermal matter (Okugawa, Sedvall, & Agartz, 2003). Also, correlations between cognitive symptoms, clinically defined as neurological soft signs (NSS), and cerebellar volumes were found (Szeszko et al., 2003). Patients with smaller cerebral volumes scored higher on scales testing the severity of NSS; conversely, healthy controls scored lower than patients with schizophrenia (Heuser, Thomann, Essig, Bachmann, & Schroder, 2011; Janssen et al., 2009).

In addition to the cerebellum, Lodge and Grace (2007) suggest an involvement of the hippocampus in the pathology of schizophrenic patients. They propose that hippocampal irregularities might play a role in the dysregulation of subcortical dopamine system functioning, which could lead to positive symptoms such as hallucinations in patients suffering from psychosis or schizophrenia. Evidence seems to supports the possibility that the ventral portion of the hippocampus is involved in the activation of dopamine neurons in response to the environment. The ventral hippocampus projects to the nucleus accumbens, which in turn inhibits the activity of the ventral pallidum. Inhibition of the ventral pallidum is linked to the eliciting of higher amplitudes in the phasic dopamine signal, leading to an increase in dopamine (Floresco, Todd, & Grace, 2001). Lodge and Grace (2007) suggested that in schizophrenic patients, the function of ventrally located GABAergic interneurons in the hippocampus is impaired, rendering the hippocampus hyperactive when confronted with environmental stimulation. The inability to inhibit the hippocampus, due to structural abnormalities, could lead to elevated levels of limbic hippocampal activity, and result in higher dopamine levels (Grace, 2012). Kapur (2003) suggests that higher dopamine concentrations could in turn lead to positive symptoms, such as hallucinations and delusions, in patients

suffering from psychosis or schizophrenia. Dopamine is seen as a mediator in the assignment of salience to experienced events. If the phasic release of dopamine becomes greater, the patient is not able to discriminate and attribute the right level of salience to transient events, termed aberrant salience. This leads to an abnormal level of phenomenological attribution in the importance of a certain mundane aspect of the patients' life.

Although involvement of the hippocampus in schizophrenia remains controversial, evidence seems to support the notion of reduced hippocampal volumes in schizophrenia. A review by McCarley et al. (1999) suggests that the parahippocampal gyrus, the entorhinal cortex and the hippocampus show reduced volumes in 77% of the studies reviewed. Additionally, Sanfilipo et al. (2002) found correlations between reduced grey matter, but not white matter, volume in hippocampal regions and cognitive performance in patients, indicating an involvement of the hippocampus in schizophrenia.

Given these previous findings, the current research explores the possibility of volumetric differences in the hippocampal grey matter, and cerebellar white and grey matter. Using a 3-dimensional manual segmentation method, the structural volumes of schizophrenic patients and healthy controls were acquired and subsequently contrasted. Findings are expected to replicate previous findings; showing lower volumes of cerebellar and hippocampal matter in patients (Honea, Crow, Passingham, & Mackay, 2005; Loeber et al., 2001; Weinberger et al., 1979), as well as reduced white/grey matter ratios in the cerebellum.

METHODS

Participants

Table 1. Statistical parameters for group characteristics.

	Schizophrenia (n = 19)	Healthy controls (n = 30)	Independent t test	
	Mean (SD)	Mean (SD)	t(df)	p
Gender	8 Male / 11 Female	19 Male / 11 Female	-	-
Age (years) [a]	26.5 (6.1)	24.5 (3.4)	1.48 (47)	0.15
BMI [b]	27.9 (4.7)	24.3 (3.3)	-2.92 (29)	0.01*
Weight (kg)	83.1 (17.7)	73.0 (14.6)	-2.18 (47)	0.04*
Height (cm)	172.3 (8.6)	172.8 (9.8)	0.18 (47)	0.86
Chronicity (years)	3.3 (3.8)	0.0 (0.0)	-	-
Medication [c]	14.0	0.0	-	-

[a] Age at time of scan. [b] Body Mass Index: mass (kg)/(height (m))^2. [c] Atypical antipsychotics.
* Significant group difference at $p < 0.05$.

Nineteen adults diagnosed with first episode psychosis (n=8), early phase psychosis (<5 years) (n=7) or established schizophrenia (>5 years) (n=4) were recruited from the Nova Scotia Early Psychosis Program (NSEPP), Halifax, Canada. Diagnosis was provided by the treating psychiatrist and was done using DSM-IV criteria. Demographic and clinical characteristics are summarized in Table 1. Thirty healthy controls were recruited through advertisements on posters and websites. Before admittance, healthy controls were screened for possible psychiatric history using

the Structured Clinical Interview for DSM-IV (SCID) (First, Gibbon, Spitzer, & Williams, 2002). Exclusion followed when participants were diagnosed with an axis I disorder, or if a first-degree relative was diagnosed with psychosis or bipolar disorder. Participants were also excluded if they had more than minimal experimentation with illicit drugs (less than 10 occasions of drug use during life time) or a pattern of alcohol misuse. Finally, all participants had to meet the MR safety criteria. Full ethics approval was obtained from the hospital ethics board, and a written consent was obtained after information about the study was provided.

MR online acquisition protocol

Brain images were acquired using a 1.5 Tesla GE scanner and a standard eight-channel head coil. The MR imaging acquisition protocol included the following parameters: a 3D SPGR T1-weighted sequence, time of echo (TE) = 4.2 ms, time of repetition (TR) = 11.3 ms, flip angle = 20 degrees, time of inversion (TI) = 500 ms, field of view (FOV) = 25.6 cm, matrix = 256 x 256 pixels, inter-slice gap = 0 mm and 170 axial slices with a 1 mm isotropic resolution.

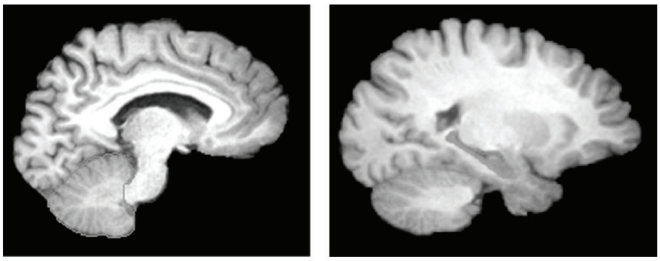

Figure 2. Sagittal plane illustrating the manual segmentation of the cerebellum (on the left) and the automatically segmented hippocampus (on the right).

Offline volumetric measurements

Using FSL software version 5.0.4 (FMRIB's Software Library), volumetric measures were acquired. During the delineation process, researchers were kept blind with regards to participants' group membership. First, brain matter was extracted using FSL's integrated BET procedure (Brain Extraction Tool, Bias Field & Neck Clean-up) (Smith, 2002). The output images were carefully examined for residual tissue, which was manually removed when present (special attention was given to eye, bone and neck areas, including the dura mater). Next, subcortical structures (including the hippocampus) were registered to the standard shape model, and subsequently segmented using the FIRST procedure (FMRIB's Integrated Registration & Segmentation Tool) (Patenaude, Smith, Kennedy, & Jenkinson, 2011) (Fig. 2). Finally, segmentation of grey matter, white matter and cerebrospinal fluid was performed using FSL's automated FAST procedure (FMRIB's Automated Segmentation Tool), a tool used to differentiate between different tissue types in 3D brain images (Zhang,

Brady, & Smith, 2001). FSLstats was used to calculate the final volumetric measures (voxel count, mm^3).

Manual delineation of the cerebellum

Using the automatically segmented images of the brain, fully manual segmentation of the cerebellum was performed. This experimenter-driven approach is the gold standard in volumetric studies (Tae, Kim, Lee, Nam, & Kim, 2008). Manual segmentation was based on images of the Human Brain Anatomy Atlas (Damasio, 2005) in order to ensure valid and consistent judgment across brains. First, the cerebellar hemispheres were separated using mainly the coronal view. The interhemispheric fissure was used as a central guideline in establishing a distinct border between the right and left half of the cerebellum. Second, the sagittal view was used to delineate the rest of the cerebellum. Starting from the most medial slice, the delineation process followed in the lateral direction demarcating voxels outlining the cerebellum. The small line of cerebrospinal fluid located superiorly to the cerebellum was used as the main landmark to separate the cerebellum from the cerebrum (Fig. 2).

Manual delineation of the cerebrum

The cerebrum was segmented, employing automated and manual methods similar to the procedure used in the delineation of the cerebellum. All brain structures located superiorly to the pons were included. The delineated cerebellar matter was excluded from the segmentation. Using the sagittal view, excessive cerebrospinal fluid was removed. The cerebrum was used as a covariant to assess whether the group differences in cerebellar and hippocampal volumes were not due to a general difference in brain size, but because of actual volumetric differences in the structures of interest. The cerebrum was chosen over the whole brain because it does not include the cerebellum structure itself, providing a more valid covariate.

RESULTS

Demographics & clinical characteristics

Independent sample t-tests were used to assess potential group differences in age, BMI, weight and height at time of scan (Table 1). No significant differences were found for age and height; however, the Body Mass Index (BMI) showed significant differences, which were driven by heavier weight in patients.

Table 2. Linear correlations between structures of interest and total cerebrum volume (voxel count).

	Pearson (parametric)						Spearman (non-parametric)					
	Schizophrenia (n = 19)			Healthy controls (n = 30)			Schizophrenia (n = 19)			Healthy controls (n = 30)		
	r	r^2	p	r	r^2	p	r	r^2	p	r	r^2	p
Cerebellum												
Total	0.61	0.37	0.006	0.82*	0.67	0.000	0.38	0.14	0.110	0.80*	0.64	0.000
Left	0.67*	0.45	0.002	0.78*	0.61	0.000	0.51	0.26	0.026	0.79*	0.62	0.000
Right	0.51	0.26	0.025	0.83*	0.69	0.000	0.33	0.11	0.175	0.82*	0.67	0.000
Cerebellum GM												
Total	0.49	0.24	0.035	0.73*	0.54	0.000	0.30	0.09	0.209	0.75*	0.56	0.000
Left	0.53	0.28	0.020	0.71*	0.50	0.000	0.31	0.10	0.204	0.73*	0.53	0.000
Right	0.42	0.18	0.074	0.73*	0.54	0.000	0.21	0.04	0.363	0.71*	0.50	0.000
Cerebellum WM												
Total	0.65*	0.43	0.003	0.75*	0.56	0.000	0.55	0.30	0.015	0.71*	0.50	0.000
Left	0.65*	0.43	0.003	0.75*	0.56	0.000	0.51	0.26	0.027	0.68*	0.46	0.000
Right	0.62	0.38	0.004	0.73*	0.54	0.000	0.51	0.26	0.025	0.69*	0.48	0.000
Hippocampus												
Total	0.34	0.12	0.150	0.63*	0.40	0.000	0.27	0.07	0.270	0.68*	0.46	0.000
Left	0.31	0.10	0.204	0.54*	0.29	0.002	0.35	0.12	0.141	0.62*	0.38	0.000
Right	0.34	0.12	0.153	0.60*	0.36	0.001	0.32	0.10	0.183	0.61*	0.37	0.000

Note. GM, grey matter. WM, white matter. *A Bonferroni correction (12 comparisons) set the alpha value at < 0.004.

Associations between volumetric variables

Pearson and Spearman correlations were computed within each group in order to search for associations between volumes (voxel count, mm^3). The total cerebrum volume was correlated with each of the following structures: total cerebellum matter volume, cerebellum grey and white matter volumes, left and right cerebellum volumes as well as corresponding grey and white matter volumes, hippocampus total matter volume, and right and left hippocampal grey matter volumes. A Bonferroni correction for multiple comparisons set the alpha value at $\alpha = 0.004$ (Table 2).

In healthy controls, parametric and non-parametric correlations yielded a similar pattern of associations, thus removing the possibility of leverage data points on the value of Pearson's correlations. As expected, healthy volunteers displayed moderate to strong linear associations between cerebrum total volume and a) total cerebellum matter volume, as well as grey and white matter volumes, b) total cerebellum left and right volumes, as well as corresponding gray and white matter volumes, and c) hippocampus grey matter volume, as well as right and left grey matter volumes (Table 2). Conversely, in patients, parametric and non-parametric correlations yielded a different pattern of associations. This indicates a likelihood of outliers in the patients' subgroup. We therefore opted for Spearman's correlations due to this possible monotonic relationship. The group of patients displayed none of the expected associations between the volumetric measures (Table 2).

Group difference in association patterns

Excel was used to analyse the data using a Fisher's Z-transformation statistic. First, acquired correlations (Table 2) were standardized using the Fisher's Z transformation. Next, the standardized correlation coefficients were compared between groups for cerebrum total volume on the one hand and cerebellum total,

cerebellum GM, cerebellum WM or the total hippocampus for both the right and the left side on the other hand (Table 3). A significant group difference in association patterns were found for the cerebellum (Z = -2.21, p = 0.027), which was mainly observed in the right side (Z = -2.58, p = 0.010). In addition, cerebellar differences in associations with the total cerebrum were mainly driven by grey matter tissue (Z = -2.10, p = 0.036). A trend was observed for group differences in associations between the total hippocampus and cerebrum volume (Z = -1.75, p = 0.080).

Table 3. Fisher's Z transformation was used to standardize the r values obtained with the Spearman correlation. In addition, a Z test was used to asses the statistical significance of the difference in associations between patients suffering from schizophrenia and healthy controls.

	$r_{patient}$ (n = 19)	$r_{control}$ (n = 30)	Z	p
Cerebellum				
Total	0.38	0.80	-2.21	0.027*
Left	0.51	0.79	-1.61	0.107
Right	0.33	0.82	-2.58	0.010*
Cerebellum GM				
Total	0.30	0.75	-2.10	0.036
Left	0.31	0.73	-1.93	0.054
Right	0.21	0.71	-2.14	0.032
Cerebellum WM				
Total	0.55	0.71	-0.85	0.395
Left	0.51	0.68	-0.84	0.401
Right	0.51	0.69	-0.90	0.368
Hippocampus				
Total	0.27	0.68	-1.75	0.080
Left	0.35	0.62	-1.14	0.254
Right	0.32	0.61	-1.20	0.230

Note. GM, grey matter. WM, white matter. * = Significant result after Bonferroni correction.

Group differences in cerebellar volumes

Given the strong associations found in healthy controls between cerebrum and cerebellum volumes (Table 2), we opted for a covariance approach to assess group differences in cerebellum volumes. Therefore, a one-way analysis of covariance (ANCOVA) was computed including the following factors: two levels for the group factor (patient and healthy control), anatomical voxel count (mm^3) of manually segmented cerebellum as the dependent variable, and total cerebrum volume as the covariate factor. The Levene's test for equality of error variances between the two groups was not significant, $F(1, 47) = 0.56$, $p = .457$. The ANCOVA revealed no group difference, $F(1, 46) = 1.66$, $p = 0.204$. Second, a multivariate analysis of covariance (MANCOVA) was used to assess potential group differences in volumes of cerebellum grey and white matter, covaried for cerebrum total volume. The multivariate test showed no significant group differences, Wilks' $\Lambda = 0.954$, $F(2, 45) = 1.07$, $p = 0.348$. Descriptive parameters are presented in Table 4.

Group differences in right and left cerebellar volumes

An analysis of group differences between right and left cerebellar volumes, covaried for cerebrum total volume, was conducted using a MANCOVA (Table 4). The

multivariate test revealed no group differences, Wilks' $\Lambda = 0.962$, $F(2, 45) = 0.90$, $p = 0.414$. Another MANCOVA was computed to assess potential group differences in right and left cerebellum volumes of grey or white matter, covaried for cerebrum total volume. The multivariate test showed no group differences, Wilks' $\Lambda = 0.950$, $F(4, 43) = 0.566$, $p = 0.688$ (Table 4).

Group differences in hippocampal volumes

A significant association between cerebrum and hippocampal volumes was found (Table 2); therefore, a one-way analysis of covariance (ANCOVA) was conducted to assess group difference in hippocampal volumes (automatically segmented), covaried for cerebrum total volumes. The Levene's test for equality of error variances was not significant, $F(1, 47) = 0.22$, $p = .638$. The ANCOVA revealed no group differences, $F(1, 46) = 0.94$, $p = 0.338$. Descriptive parameters are presented in Table 4.

Table 4. Means (standard deviations) for cerebrum, cerebellum and hippocampus volumes (voxel count, cm^3).

	Schizophrenia (n = 19)			Healthy controls (n = 30)		
	Right	Left	Total	Right	Left	Total
Cerebrum						
Total	-	-	1257.9 (92.7)	-	-	1271.4 (135.8)
GM	-	-	553.2 (45.1)	-	-	565.4 (59.3)
WM	-	-	459.0 (37.1)	-	-	462.2 (58.2)
Cerebellum						
Total	71.4 (5.6)	71.9 (5.4)	143.3 (10.7)	73.8 (7.3)	73.9 (7.5)	147.7 (14.5)
GM	32.8 (2.7)	32.4 (2.5)	65.2 (5.0)	34.0 (3.7)	33.7 (3.6)	67.8 (7.3)
WM	26.3 (2.0)	26.8 (2.4)	53.1 (4.3)	27.0 (3.4)	27.4 (3.4)	54.3 (6.7)
Hippocampus						
Total	3.8 (0.5)	3.7 (0.4)	7.4 (0.9)	3.9 (0.5)	3.8 (0.5)	7.7 (0.8)

Note. GM, grey matter. WM, white matter.

Group differences in right and left hippocampal volumes

The effect of group on left and right hippocampal volumes, covaried for cerebrum total volume, was tested using a MANCOVA (Table 4). The multivariate test showed no group difference, Wilks' $\Lambda = 0.980$, $F(2, 45) = 0.47$, $p = 0.631$.

DISCUSSION

The current study investigated whether there is a difference in structural volume between schizophrenic patients and healthy controls. In order to find volumetric differences in cerebellar and hippocampal volumes we first gathered T1-weighted MR images in a sample of patients suffering from first episode psychosis, early phase psychosis or established schizophrenia and healthy controls. Subsequently, to determine whether structural differences were present, cerebellar and hippocampal

volumes were contrasted between groups. By using the cerebrum total volume as a covariant, we were able to control for the random variability in human brain size due to height and mass differences in participants. Furthermore, we computed the correlations between the acquired cerebrum volume (voxel count) and the hippocampal and cerebellar delineated volumes. In addition, we determined whether there was a group difference between acquired association patterns.

Findings revealed no significant volumetric differences in relative voxel count (mm^3) between healthy controls and schizophrenic patients, in the cerebellum, cerebellar grey and white matter, or the hippocampus. However, the associations between total cerebrum volumes and cerebellum or hippocampus volumes showed opposite results between groups. As proposed *a priori*, parametric and non-parametric tests showed a moderate to strong linear association in healthy controls (Table 2). Conversely, in the patients group, parametric and non-parametric tests showed a different pattern of associations. We therefore decided to use a non-parametric approach to adjust for the possible leverage points. Contrasting healthy controls, the data from patients showed no significant correlations between the cerebrum volume, and hippocampal and cerebellar volumes in schizophrenic patients. This could indicate abnormalities in the proportions of the hippocampus and cerebellum relative to the total cerebrum, existing only in patients but not healthy controls. Especially cerebellar grey matter seemed to be affected in schizophrenic patients (Table 2). Furthermore, the data shows the group difference in associations to be significant for the hippocampal and cerebellar matter relative to the total cerebrum. The group differences in cerebellar association with cerebrum volume seemed to be driven by grey matter, and were mostly apparent on the right cerebellar side (Table 3). A significant group difference in correlations adds to the possibility of a contrast in the ratio between the volume of the cerebrum and the investigated structures in patients relative to healthy controls, denoting a possibility for volumetric abnormalities in patients.

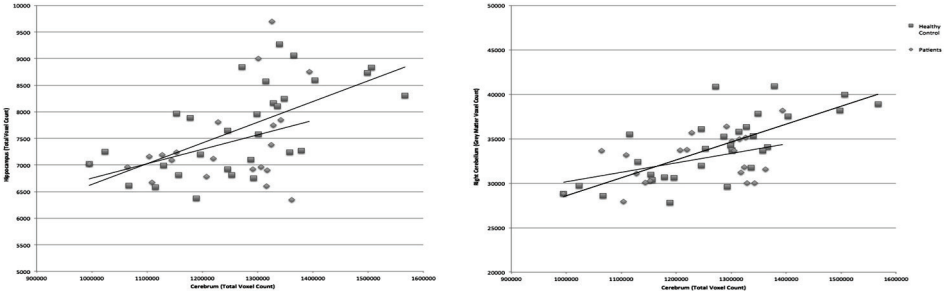

Figure 3. Spearman and Pearson correlations were calculated to determine whether hippocampal and cerebellar structures were significantly associated in patients and healthy controls. Both correlations between Hippocampal GM and Cerebrum Total as well as Right Cerebellum GM and Cerebrum Total were significant for the healthy control group. No significant correlations were found for the patient group. A significant difference was found in correlations between both groups, indicating possible structural abnormalities in the hippocampal and cerebellar volumes of patients suffering from schizophrenia.

Results seem to support a lack of association between the structures of interest and the cerebrum in patients, implying possible structural abnormalities in the hippocampal and cerebellar volumes (Table 3). The difference in the cerebellum was especially apparent on the right side, and was mainly driven by grey matter differences (Fig. 3). The finding of abnormalities in the structural volume of cerebellar and hippocampal matter is consistent with a large body of evidence (Ichimiya et al., 2001; Keller et al., 2003; Lee et al., 2007; Loeber et al., 2001; Lungu et al., 2013). Research indicates an asymmetry in the cerebellum, with lower volumes on the right as compared to the left (Levitt et al., 1999). Different lines of research show a parallel between the increase of cognitive symptoms and a decrease in cerebellar volumes in schizophrenia (Andreasen & Pierson, 2008). For example, Szeszko et al. (2003) showed that neuropsychological functions, including visuospatial awareness, executive functioning, and memory, were impaired in patients but not in healthy controls. Additionally, the decline in neurological functioning was associated with a decline in cerebellar volume. Again, increases in NSS were most apparent when the right side of the cerebellum showed reduced volumes (Bottmer et al., 2005).

A large body of research, focussing on the volumetric properties of the cerebellum in schizophrenia, has shown that the cerebellar vermis is mainly compromised in patients (Loeber et al., 2001; Okugawa et al., 2007). This reduction in cerebellar vermis volume has been linked to affective as well as cognitive deficits, although impaired cognition is mainly observed when other parts of the cerebellum have also been affected (Schmahmann, 2004; Schmahmann & Pandya, 1997; Tavano et al., 2007). Vermal abnormalities are also evident in congenital neurodevelopmental disorders such as Dandy Walker malformation (Klein, Pierre-Kahn, Boddaert, Parisot, & Brunelle, 2003) and Joubert syndrome (Saraiva & Baraitser, 1992). Currently, evidence is accumulating rapidly, implying an important role of the cerebellar vermis in schizophrenia (Lawyer, Nesvag, Varnas, Okugawa, & Agartz, 2009; Okugawa et al., 2003). Interestingly, a higher prevalence of excessive white mater seems to manifest itself in male patients, as opposed to female patients (Lee et al., 2007; Okugawa et al., 2002).

The ability to learn new information, as well as retrieval of episodic and semantic memory, is also impaired in schizophrenic patients (Holthausen et al., 2003). Research by Egeland et al. (2003) showed that these abnormalities are the result of problems in encoding processes. This is different in depressed patients, who mainly show difficulties in the retrieval process (Veiel, 1997). Problems in memory, especially with regards to encoding processes, have been linked to structural differences located in the medial temporal lobe (Boyer, Phillips, Rousseau, & Ilivitsky, 2007). In schizophrenia, research shows that especially the hippocampal structure is impaired. A meta-study by Nelson, Saykin, Flashman, and Riordan (1998), in which 18 studies were compiled, showed a bilateral decrease of 4% in hippocampal volume. In addition, a more recent meta-study involving 300 patients and 287 healthy controls showed an 8% decrease in both left and right hippocampal volume (Steen, Mull, McClure, Hamer, & Lieberman, 2006).

In conclusion, our results seem to confirm a trend towards an abnormal volumetric pattern in both the cerebellum and the hippocampus. These findings, combined with earlier volumetric and functional research in schizophrenia seem to indicate these structures in schizophrenic pathology.

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MATTHIAS VOSS

Chased by Wolves: Effects of a Threat Prime on Working-Memory in Portuguese and Hong Kong Populations

Original Paper

Cultural differences between Western and East Asian populations have been categorized in terms of Individualism versus Collectivism. This study investigates the role of working memory and a threat prime across these cultures. Therefore, 30 participants from Hong Kong and 26 participants from Portugal were compared. Individualism and Collectivism levels were measured using the Auckland Individualism and Collectivism Scale (Shulruf, Hattie & Dixon, 2007). Working memory was tested using the Corsi block-tapping task (Corsi, 1972). Finally, a modified version of the wolfpack task (Gao, McCarthy & Scholl, 2010) was employed to investigate analytic / holistic perception, perceived animacy, and changes in working memory after a threat prime. An interaction between priming condition and culture was found. The performance of the Hong Kong group stayed constant over both conditions, while the performance of the Portuguese group deteriorated after a threat prime. While Hong Kong scored higher on Collectivism, no difference between the two cultures was found for Individualism. In addition, no correlation was found between Collectivism and working memory performance after threat prime. The wolfpack task used here proved insufficient to detect differences in analytic and holistic perception across cultures. This study urges caution when applying the Individualism-Collectivism distinction to these cultures.

Keywords: Working Memory, Collectivism, Individualism, Wolfpack Task

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INTRODUCTION

In his influential 1980 book *Culture's consequences: International differences in work- related values*, Hofstede divided cultures along a collectivistic – individualistic spectrum. He found Western cultures to be individualist, while East Asian cultures were collectivist. Indeed, researchers have found differences between Western and East Asian cultures to be so profound that, according to Nisbett, Peng, Choi, and Norenzayan (2001) "Psychologists who choose not to do cross-cultural psychology may have chosen to be ethnographers instead" (p.307). However, a meta-analysis by Oyserman, Coon and Kemmelmeier (2002) found that differences in individualism and collectivism across cultures were not as extreme as suggested. They found that European Americans fitted the description of an individualist society by scoring both high on individualism and low on collectivism. In contrast, they found that for East Asian populations, Chinese society fitted the classical description of a collectivist society the best by both scoring low on individualism and high on collectivism. While the individualism-collectivism distinction remains influential, they found that other East Asian cultures did not fit this pattern as nicely (Oyserman et al., 2002). Still, whether one grows up in a Western or in an East Asian culture may influence how one thinks about the world (Nisbett & Masuda, 2003; Lim, 2007; Lim & Giles, 2007) and about oneself (Markus & Kitayama, 1991). For example, Westerners perceive the world according to attitudes, beliefs and personality of the individual, while East Asians use in-group norms, context, and history of events to make sense of the environment (Morris & Peng, 1994). Furthermore, Westerners see themselves separate from the social context, and put emphasis on private achievements, expressing oneself and being unique. In contrast, East Asians see themselves as part of the group, and put emphasis on public tasks, fitting in, and being a good member of society (Markus & Kitayama, 1991). Thus, individualists are more independent, while collectivists are more interdependent.

In parallel to the Individualism-Collectivism distinction, differences in world view, cognition, perception and attention across cultures have often been described as analytic for Westerners and holistic for East Asians (e.g. Lim, 2007; Lim & Giles, 2007; Masuda & Nisbett, 2001; Nisbett et al, 2001; Nisbett & Masuda, 2003; Nisbett & Miyamoto, 2005, Miyamoto, Nisbett & Masuda, 2006). The analytic worldview is described as trying to find key elements and relationships in the bigger world, thus breaking it up into smaller parts (Kim, Lim, Dindia & Burrell, 2010). In contrast, the holistic worldview is described as seeing everything as a whole without breaking it into smaller parts (Kim et al., 2010) Similarly, there exist different cognitive strategies to cope with the environment: Westerners tend to make more use of categorical, rule-based thinking and formal logic, compared to East Asians (Nisbett et al, 2001, Nisbett & Masuda, 2003). Conversely, East Asians make more use of dialectical reasoning and causal attributions (Nisbett et al, 2001, Nisbett & Masuda, 2003).

But apart from cognition, basic perceptual and attentional processes were also found to differ. In one classic experiment, Masuda and Nisbett (2001) showed Japanese and American participants animated underwater scenes, which consisted of a salient fish in the foreground, and other fish and marine life in the background. The participants had to remember the scene and then make statements about it. They found that Japanese perceived and remembered objects in relation to their contexts better and paid more attention to interrelations between objects. In contrast, Americans perceived objects relatively independent of their field. These findings supported the analytic-holistic distinction. Westerner's perception is more analytic, meaning they focus more on highly salient single objects and their properties. In contrast, East Asians, who come from collectivist cultures, have a more holistic perception. They take into account various objects, their interrelations, and not so salient background stimuli. Their perception is more focused on the broader picture. (Ji, Peng & Nisbett, 2000; Nisbett & Miyamoto, 2005; Masuda & Nisbett, 2001 Miyamoto et al., 2006) Furthermore, Savani and Markus (2012) have proposed that selective attention may also play a role in this distinction, making it easier for Westerners to discern important from unimportant stimuli due to their analytic attention style.

Interestingly, holistic and analytic perception styles may already be present at an early age. In a recent study, Senzaki, Masuda and Nand (2014) compared landscape paintings and collages of Canadian and Japanese school children from grades one through six. They found that while in grade one the paintings were relatively similar, with increasing age the paintings were increasingly conforming to holistic ideologies for Japanese children, and to analytic ideologies for Canadian children. This supports the notion of analytic and holistic perception emerging from distinct cultural backgrounds.

In summary, East Asian cultures have been characterized as collectivistic, meaning they are more interdependent and put emphasis on belonging to their group (Markus & Kitayama, 1991). They have also been labeled holistic, which means seeing interrelations between different objects, and considering their contexts and the scene as a whole (e.g. Nisbett & Miyamoto, 2005). Conversely, Westerners are thought to be individualistic, being more independent and putting emphasis on personal achievements and uniqueness (Markus & Kitayama, 1991). Additionally, they have been labeled analytic, which means they break up the whole picture into smaller parts, and analyze each object relatively independent of their surroundings (e.g. Nisbett & Miyamoto, 2005).

In the current study, we built on this work, and compared Portuguese and Hong Kong populations. The cultural differences mentioned above have been most extensively researched between American and Japanese cultures (e.g. Masuda & Nisbett, 2001, Miyamoto et al., 2006) or American and Mainland Chinese cultures (e.g. Ji et al., 2000). The purpose of choosing Portugal and Hong Kong as cultures to be compared was to see if these findings also hold true for less extensively researched Western and East Asian cultures. Therefore, the current experiment was also set up to investigate how easily the individualism/collectivism distinction and the analytic/holistic distinction could be generalized to other Western and East Asian cultures. Most East Asian cultures that were categorized by Hofstede (1980)

to be collectivist, have been found to show holistic cognition and perception (e.g. Nisbett et al., 2001, ; Nisbett & Masuda, 2003; Nisbett & Miyamoto, 2005). Similarly, cultures categorized as individualistic showed analytic cognition and perception (e.g. Nisbett et al., 2001, ; Nisbett & Masuda, 2003; Nisbett & Miyamoto, 2005). The Portuguese and Hong Kong populations in this study were also compared on their levels of individualism and collectivism, as well as their degrees of analytic or holistic perception.

Additionally, cultural differences in working memory were researched. Working memory is defined as a part of short-term memory that is responsible for keeping important things in mind while performing complex tasks (Baddeley, 2010). Compared to perception and attention, little is known about working memory differences across cultures. While the literature on this topic is not very extensive, insight comes from a study by Imbo and LeFevre (2009). They compared Chinese, Belgian and Canadian participants on the effects of working-memory load on math problem solving. They found that Chinese participants were faster than Belgians and Canadians, and also required fewer working memory resources. The Authors attributed these effects to different cultural backgrounds, and different forms of education during childhood. In this study, we compared Portugal and Hong Kong populations on working memory, and investigated the effect of a threat prime on working memory performance. The threat prime was also used to see if this affects how people react to their ingroups or outgroups. Specifically, approach and avoidance behavior to the participant's ingroup and outgroup was measured.

We hypothesized that the two populations would differ significantly on individualism and collectivism. Consistent with prior research, we expected Portugal to score higher in individualism, as it is a western culture. Additionally, we expected Hong Kong to score higher on collectivism, as it is an East Asian culture. Similarly, we hypothesized that Portugal would show higher levels of analytical perception, and that Hong Kong would show higher levels of holistic perception. Furthermore, we expected that the two cultures would show different response patterns in the wolfpack task after being confronted with a threat prime. Considering working memory, building on the findings of Imbo and LeFevre (2009), we predicted that Hong Kong would score higher than Portugal, both in normal tasks, and after a threat prime.

METHODS

Participants

The experiment was approved by the local ethical committees. There were 68 participants in total. 30 of them were local Portuguese students of the University of Lisbon (mean age = 21.8), while the other 38 were local Hong Kong students of the Chinese University of Hong Kong (mean age = 19.8). Out of the 38 participants from Hong Kong, 8 were male and 30 were female. The 30 Portuguese participants consisted of 14 males and 16 females. All students were undergraduate students,

and a pre-experimental screening was performed via a short questionnaire sent by email. Its purpose was to make sure that participants (1) had no vision impairments, (2) had no memory impairments, and (3) were born and raised in Portugal or Hong Kong and spent the greatest part of their life there, to make sure that they were shaped by the respective cultures this experiment claims to compare. For their participation, they received a compensation of 7 Euros or 75 Hong Kong Dollars.

In total, 12 participants had to be excluded from the analysis. 10 exclusions were due to technical difficulties. The program crashed, and as a result not enough trials were obtained to guarantee a proper analysis or counterbalancing. The remaining participant was excluded because contrary to answers on the per-experimental screening, the participant had not grown up exclusively in an East Asian culture. The last excluded participant was an outlier, and was excluded because the participant's responses indicated a complete disregard of task instructions, pressing the same button 99 percent of the time. All excluded participants were still fully compensated. After these exclusions, there were 30 participants in the Hong Kong group (5 male and 25 female) and 26 in the Portuguese group (13 male and 13 female).

Materials

Auckland Individualism and Collectivism Scale (AICS)

To measure collectivism and individualism of the participants, we employed the Auckland Individualism and Collectivism Scale, short AICS, which was developed by Shulruf, Hattie and Dixon (2007). This questionnaire defines three dimensions of individualism: responsibility, uniqueness and competitiveness, and two dimensions of collectivism: advice and harmony. Participants had to rate 26 statements on the frequency (1= never to 6= always) they behave in the given ways. 15 statements load on the individualism dimensions, while 11 questions load on the collectivism dimensions.

Corsi Block Tapping Task

To measure spatial working memory in a standardized way, a digital version of the Corsi block tapping task was used (Corsi, 1972; Berch, Krikorian & Huha, 1998). The task was run via Millisecond software's Inquisit 4 (2012). In this task, an increasing number of blocks were displayed, and then highlighted in a specific order. The participant had to remember the order of highlighting, and click the blocks in the same sequence (Corsi, 1972,). The task started with two blocks, and gradually increased the number of lit-up blocks to nine. The participant had to complete each number of blocks correctly twice before continuing the task with more blocks. If the participant failed twice in a row, the task ended and the participant's score was provided. This task was needed to see whether differences in the memory task performed afterwards could be explained with working memory capacity, or had alternative explanations.

Wolfpack task with integrated working memory task and approach-avoidance task

To investigate the differences in perception, and in order to provide the threat prime, the so-called "wolfpack effect" (Gao, McCarthy & Scholl, 2010) was used. This effect worked with perceptual animacy, which means that people attribute social interactions and intentions to objects, based on motion cues (Meyerhoff, Huff & Schwan, 2013). Participants saw a video with some darts and a square in it. All the objects were moving around in a completely random manner. In one condition, each dart was always oriented perpendicular to the square, thus not facing it. But in the other condition, the "wolfpack condition", each dart constantly faced the square. Even though each dart's movement was completely random, the fact that they were constantly facing the square made it seem as if they were chasing it, like a pack of wolves (see figure 1).

In order to guarantee a smooth experiment, the remaining tasks for chase perception, working memory and approach-avoidance behavior were aggregated into one continuous task. The video stimuli and the code for this task were custom-made by the researchers, and were run using the free open-source software Psychopy (Pierce, 2007).

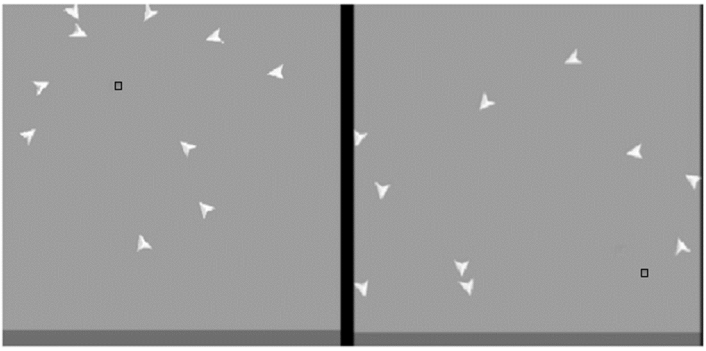
In this task, participants first saw a video of a square and ten dart-shaped objects moving around. At the end of the video, the scene froze for two seconds so participants could remember it. The darts were either arranged perpendicular, thus facing away from the square, or they were constantly facing the square. This latter condition was the wolfpack condition that created a perception of animacy.

After seeing the video of either the perpendicular or the wolfpack condition, people had to indicate whether or not they thought the darts were chasing the square. They did so by clicking the left or right mouse button, respectively. As the perception of a chase depends on the interaction of many moving objects, this effect should give an indication of the participant's degree of analytic or holistic perception.

Afterwards, they saw a picture which was either an exact screen shot of the end of the video they just saw, or a slightly manipulated picture. They had to indicate if it was the same or a different picture by pressing the left or right mouse button again. This served as a working memory test with a threat prime, to see if items would be encoded into memory more easily in threatening conditions. This reasoning follows findings by Gao et al. (2010), who successfully used the wolfpack task as a social cue. The proportion of same and different pictures the participants saw was 50/50. In the screenshots or manipulated pictures that the participants saw, the position of the "sheep" and the facing direction of the "wolves" were controlled for, so participants had to memorize the position of up to 10 wolves in order to judge if a picture was the same or different.

Finally, the participants received an instruction for the approach-avoidance task, and saw a picture of their ingroup or their outgroup afterward. The instruction either stated to move the mouse forward if the picture was turned clockwise and backward if the picture was turned counterclockwise, or the instruction was the other way around. This way, they would be focusing on which way the picture was turned, and not if their ingroup or outgroup was on the picture. The video they saw before functioned either as a threat prime (wolfpack condition), or as a control

(perpendicular condition), which should influence their movement of the mouse. The results of this approach-avoidance task are not discussed here, as this paper's focus is on working memory.



a) wolfpack orientation **b)** perpendicular orientation

Figure 1. An example of the stimuli used in the experiment. In the wolfpack condition (a) the darts were constantly facing the square, while their movement was completely random. This induced a perception of animacy. In the control condition (b), the darts were constantly oriented perpendicular to the square, while their movement was also random. For a video of moving stimuli similar to those used in this experiment, visit: http://perception.research.yale.edu/Animacy-Wolfpack/Animacy-Wolfpack-Search-Wolfpack-NoCheating.mov for the wolfpack condition and http://perception.research.yale.edu/Animacy-Wolfpack/Animacy-Wolfpack-Search-Perpen-NoCheating.mov for the perpendicular condition (Scholl,n.d.).

Procedure

The design of this study was a quasi-experimental split-plot design. The procedure was identical for Portuguese and Hong Kong students. The experiment started with a brief description, and participants filled out an informed consent form. They were also told that they may stop participating in the study at any point, should they feel uncomfortable.

After their written consent had been given, participants filled out the AICS questionnaire. Afterwards, they completed the Corsi Block Tapping task on a computer screen. Then they moved on to the Wolfpack task. This task had a 2x2 design. The wolfpack task had two conditions (wolfpack and perpendicular), and the approach-avoidance task had two conditions (approach/avoid). The working memory task embedded in this task did not add any additional conditions. Even though people could see an identical or a different picture, only the percentage of correct responses was measured. All four possible conditions were counterbalanced, and each participant completed 40 trials of each condition, so 160 trials in total (see figure 2). Furthermore, the design of this study was a mixed design. It had a between-subject factor, namely the Portuguese and Hong Kong group of participants. It also had several within-subject factors, as every subject ran through all conditions of the wolfpack/working memory/approach-avoidance task.

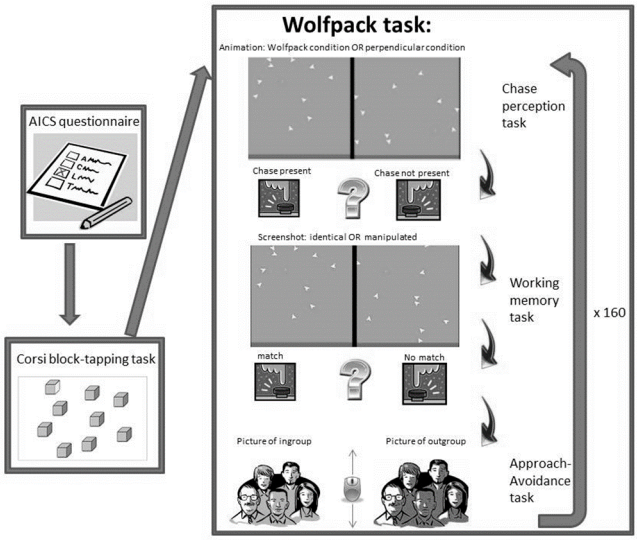


Figure 2. The procedure of this experiment. First, participants filled out the Auckland Individualism and Collectivism Scale. Afterwards, they completed the Corsi block-tapping task. Then, they moved on to the wolfpack task: Participants saw an animation in which objects were either in the wolfpack orientation (this provided the threat prime), or in the perpendicular orientation (this provided the neutral prime). The animation froze for two seconds at the end, so that participants could remember the configuration of objects. They then had to indicate via button press if a chase was present or not. Afterwards they saw a picture, which was either a screen shot, or a modified version, of the last two seconds of the video. Participants had to indicate via button press whether the picture was identical. Finally a picture of either their ingroup or their outgroup was presented. This picture was slightly rotated clockwise or anticlockwise, and instructions were given to move the computer mouse forward or backward, depending on the rotation of the picture. The whole wolfpack task was run 160 times, 80 times with a threat prime and 80 times with a neutral prime.

STATISTICAL ANALYSIS

To investigate the differences in collectivism and individualism across cultures, independent samples t-tests were performed for collectivism score and individualism score, and on each sub-category of individualism and collectivism. Significance tests were one-tailed. However, Shulruf, et al. (2011) suggested that a cluster analysis is more informative than the mean. Therefore, a k-cluster analysis was also performed. This made it possible to get an understanding of within-group variation on individualism and collectivism. Within each culture, participants were divided into four clusters, based on their scores. These clusters were: Mid Individualism- High Collectivism (MI-HC), High Individualism- Mid Collectivism (HI-MC), High Individualism- High Collectivism (HI-HC), and Mid Individualism-

Mid Collectivism (MI-MC). The cultural differences in the Corsi block-tapping task were also measured with a one-tailed independent samples t-test.

In order to investigate chase perception, we performed a split-plot ANOVA (General Linear Model). Culture served as a Between-Subject factor. The Within-subject factor was provided by the measure of chase detection. More precisely, we used the participant's score on how often they correctly identified that a chase was happening, in the perpendicular condition and in the wolfpack condition, respectively. This analysis was then repeated with the scores on individualism, collectivism, and the Corsi block-tapping task added as co-variables.

In order to investigate working memory capacity after a threat prime, we performed another split-plot ANOVA (General Linear Model). Culture served as the between-subject factor again. The within-subject factor consisted of a working memory measure after a threat prime (wolfpack condition) or after a neutral prime (perpendicular condition). Specifically, after watching either an animation of the wolfpack condition or of the perpendicular condition, participants saw either a screenshot of the animation they just saw, or a slightly different picture. They had to indicate if the picture was identical to what they had just seen during the animation. The corsi block tapping task was included as a co-variable, as it measures working memory. Furthermore, the scores on correct identification of chase in the wolfpack and perpendicular conditions were also added as co-variables, since these provided the threat primes or neutral primes.

Finally, the Corsi block-tapping task, individualism, and collectivism scores were correlated to the different conditions of the chase perception task and the wolfpack memory task.

RESULTS

Auckland Individualism and Collectivism Scale

We found significant differences between the Hong Kong and Portuguese groups for Collectivism with $t(54) = 3.49$, $p < 0.001$. As expected, the Hong Kong group scored higher on collectivism ($M = 4{,}04$, $SD = 0.58$) than the Portuguese group ($M = 3.56$, $SD = 0.44$). The two groups did not differ significantly on individualism, $t(54) = -1.17$, $p = 0.124$ (see figure 3a). An analysis of the different sub-categories of the AICS showed that scores differed on only one sub-item. This was "harmony" ($t(54) = 3.52$), $p < 0.001$), which loads on collectivism (see table 1). Cluster analysis showed that the largest cluster of Hong Kong participants (40%) had midlevel individualism scores and high collectivism scores. The second largest cluster of Hong Kong participants (30%) had high individualism scores and midlevel collectivism scores. The greatest part of the remaining participants (27%) scored high on both individualism and collectivism. In the Portuguese group, there were no participants that had midlevel score on individualism and a high score on collectivism. Instead, the biggest cluster (65%) scored high on individualism and medium on collectivism. This cluster was almost as big as the two biggest clusters from the Hong Kong group combined.

Unlike the Hong Kong participants, the largest part of the remaining Portuguese participants (31%) had midlevel scores in both individualism and collectivism (see figure 3b).

Corsi Block-Tapping Task

The Corsi block-tapping task showed a marginally significant effect between cultures ($t(54) = 1.611$, $p = 0.057$), with the Hong Kong group scoring higher than the Portuguese group ($M = 73{,}33$; $SD = 24{,}21$ for the Hong Kong group and $M = 62{,}77$; $SD = 24{,}77$ for the Portuguese group).

fig. 3a

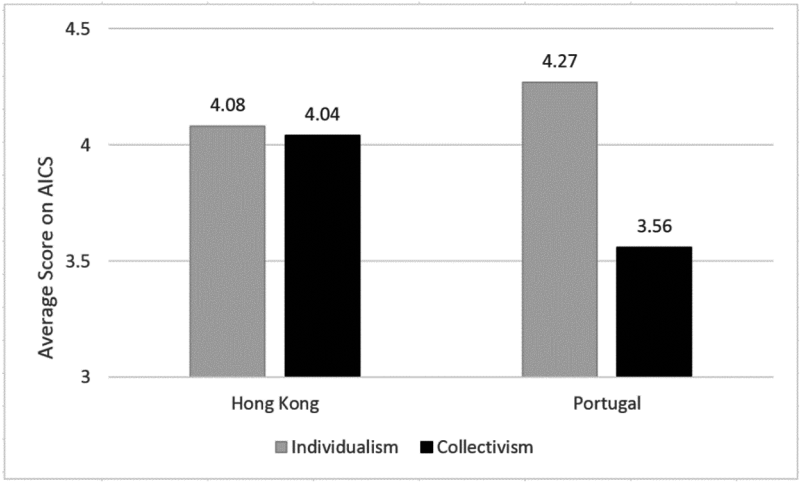


fig. 3b

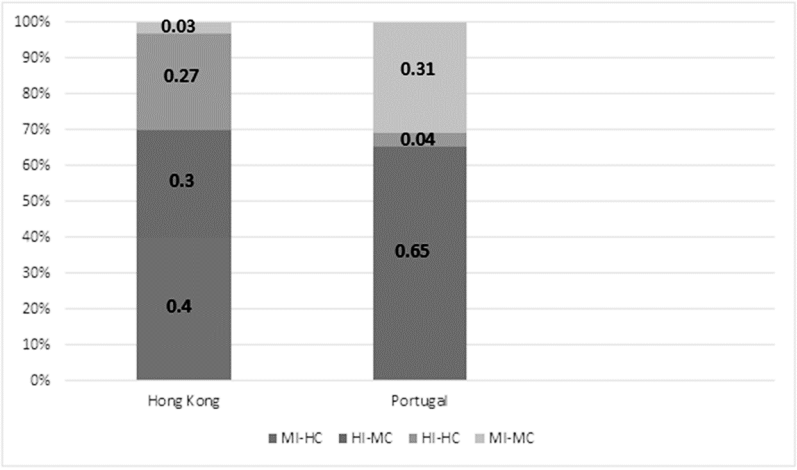


Figure 3. Individualism and Collectivism scores by culture. a) mean individualism and collectivism scores, b) cluster analysis showing percentage of people belonging to one of the following clusters: Mid Individualism- High Collectivism (MI-HC), High Individualism- Mid Collectivism (HI-MC), High Individualism- High Collectivism (HI-HC), and Mid Individualism- Mid Collectivism (MI-MC)

Table 1. Means and standard deviations on Individualism, Collectivism, and its subcategories by culture.

		Hong Kong			Portugal		
		M	SD	N	M	SD	N
Individualism	Total	4,08	0,64	30	4,27	0,5	26
	Responsibility	4,58	0,67	30	4,70	0,37	26
	Uniqueness	4,23	0,97	30	4,59	0,89	26
	Competence	3,72	0,71	30	3,51	0,87	26
Collectivism	Total	4,04	0,58	30	3,56	0,44	26
	Advice	4,19	0,73	30	3,92	0,68	26
	Harmony	3,78	0,64	30	3,17	0,65	26

Wolfpack task

Measuring perceived animacy through chase detection

In the chase detection task, we found no significant difference between cultures ($F_{1, 54} = 0.001$, $p = 0.976$), meaning that both Hong Kong and Portuguese populations perform equal on detecting whether a chase was present in the wolfpack task. However, we found a significant difference between conditions, with $F_{1, 54} = 7.292$ and $p = 0.009$. Responses were measured in a percentage score. In the perpendicular condition, the correct answer to whether a chase was present was always no, and in the wolfpack condition the correct answer was always yes. Of course, participants were unaware of this, as they did not know about the two different experimental conditions. Thus, people are better at identifying that no chase is present in the perpendicular trials ($M = 0.9$, $SD = 0.13$ for Hong Kong and $M = 0.85$, $SD = 0.16$ for Portugal) than at identifying that a chase is present in the wolfpack trials ($M = 0.79$, $SD = 0.20$ for Hong Kong and $M= 0.84$, $SD = 0.18$ for Portugal). Additionally, we found a marginally significant interaction between conditions of the wolfpack task, and culture; $F_{1, 54} = 30828$, $p = 0.056$.

When repeating the analysis with the added covariables, the within-subject effect that compared the wolfpack condition to the perpendicular condition disappeared ($F_{1, 51} < 0.001$, $p = 0.998$). The interaction also disappeared ($F_{1, 51} = 1.56$, $p = 0.217$). Furthermore, there was no significant interaction with the co-variables, neither between task conditions and Individualism score ($F_{1, 51} = 0.198$, $p = 0.279$), nor between task conditions and Collectivism score ($F_{1, 51} = 0.023$, $p = 0.881$), or task conditions and score on the Corsi block tapping task ($F_{1, 51} = 1.580$, $p = 0.214$). Furthermore, there was still no between-subject effect for culture. ($F_{1, 51} = 0.942$,

p = 0.336). While we found no between-subject effects for the Corsi block-tapping task ($F_{1, 51}$ = 0.158, p = 0.692) or for Collectivism score ($F_{1, 51}$ = 1.921, p = 0.172), we did find a between-subject effect for Individualism score ($F_{1, 51}$ = 6.041, p = 0.017). We then ran the analysis once more, but included only Individualism score as a co-variable, since this was the only significant one. There was still no within-subject effect for task condition ($F_{1, 53}$ = 1.843, p = 0.180), task condition * Individualism score ($F_{1, 53}$ = 1.004, p = 0.321) or task condition * culture ($F_{1, 53}$ = 3.149, p = 0.082), although the interaction showed a trend (see figure 4). While the between-subject effect of culture was still insignificant ($F_{1, 53}$ = 0.132, p = 0.718), the between-subject effect of Individualism score remained significant ($F_{1, 53}$ = 6.295, p = 0.015).

Then the co-variables were correlated to the chase perception task. No significant correlations were found in the Hong Kong group. In the Portuguese group, individualism correlated with both the perpendicular trials and the wolfpack trials of the chase perception task (see table 2).

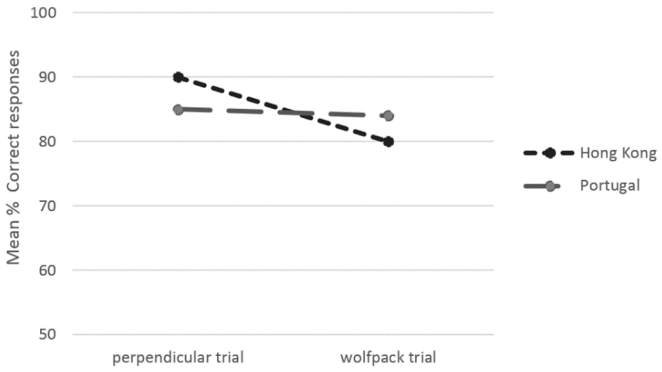


Figure 4. Mean percentage of correct identification on the chase perception task. A test for interaction was not significant (F1, 53 = 3.149, p = 0.082.)

Measuring working memory after threat prime

No main effect for the match/no match task was found; $F_{1, 51}$ = 0.084, p = 0.773. Moreover, no significant interaction was found between the match/no match task and either the Corsi block-tapping task ($F_{1, 51}$ = 1.687, p = 0.2), the chase detection in the wolfpack condition ($F_{1, 51}$ = 0.011, p = 0.916), or chase detection in the perpendicular condition ($F_{1, 51}$ = 0.524, p = 0.472).

Furthermore, a main effect for culture was found; $F_{1, 51}$ = 5.722, p = 0.020. The Corsi block-tapping task showed no significant between-subject effect ($F_{1, 51}$ = 0.4081, p = 0.777), and neither did chase perception in the wolfpack condition ($F_{1, 51}$ = 0.430, p = 0.515). Yet chase perception in the perpendicular condition showed a significant between-subject effect ($F_{1, 51}$ = 6.527, p = 0.014). Additionally, an interaction between the match/no match task and culture was found; $F_{1, 51}$ = 5.092, p = 0.028 (see figure 5).

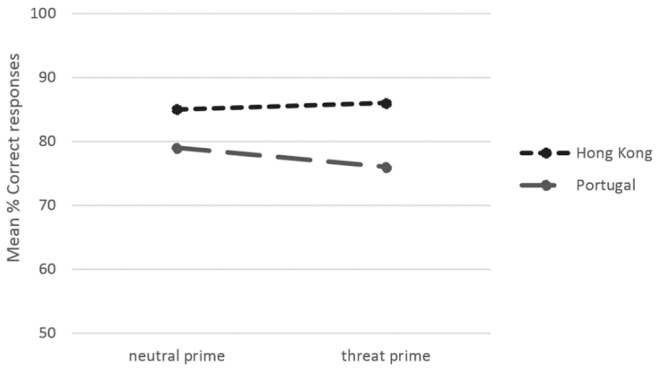


Figure 5. Mean percentage of correct answers on the match / no match task after threat prime and neutral prime per culture. A test for interaction was significant (F1, 51 = 5.092, p = 0.028).

A post-hoc analysis of simple effects showed that cultures differed significantly in the perpendicular condition of the match / no match task ($t(54) = 2.111$, $p = 0.039$, M = 0.86; SD = 0.13 for the Hong Kong group and M = 0.79; SD = 0.12 for the Portuguese group). Cultures also differed significantly in the wolfpack condition of this task ($t(54) = 3.197$, $p = 0.002$, M = 0.86; SD = 0.12 for the Hong Kong group and M = 0.76; SD = 0.12 for the Portuguese group).

Furthermore, within the Hong Kong population there was no significant difference between the wolfpack condition and the perpendicular condition of the match/no match task; $t(29) = -0.729$, $p = 0.472$, M = 0.86; SD = 0.13 for the perpendicular condition and M = 0.86; SD = 0.12 in the wolfpack condition. In contrast, the Portuguese population showed a significant difference between the two conditions of this task; $t(25) = 2.468$, $p = 0.021$. The Portuguese group performed worse in the wolfpack condition, where they saw a threat prime (M = 0.76; SD = 0.12) than in the perpendicular condition, where they saw a neutral prime (M = 0.79; SD = 0.12).

Correlating the different tasks

In the Hong Kong population, we found no correlations between either collectivism, individualism, or the Corsi block-tapping task and the match/ no match task. However, in the Portuguese population, we found a marginally significant correlation between individualism and the wolfpack condition of the match / no match task (see table 2). Furthermore, a trend could be discerned for correlations between individualism and the perpendicular condition of this task, as well as for individualism and the Corsi block-tapping task (see table 2).

Hong Kong

	Corsi block-tapping task	AICS: Individualism	AICS: Collectivism
Chase: perpendiular	r=-0,035 p=0,854	r=0,005 p=0,981	r=-0,161 p=0,394
Chase: wolfpack	r=-0,049 p=0,798	r=0,254 p=0,176	r=-0,158 p=0,405
Chase: Overall	r=-0,049 p=0,796	r=0,179 p=0,345	r=-0,183 p=0,332
Match: perpendicular	r=0,049 p=0,798	r=-0,106 p=0,579	r=-0,031 p=0,870
Match: wolfpack	r=-0,020 p=0,917	r=-0,150 p=0,430	r=-0,122 p=0,520
Match: Overall	r=0,015 p=0,936	r=-0,123 p=0,518	r=-0,068 p=0,722

Portugal

	Corsi block-tapping task	AICS: Individualism	AICS: Collectivism
Chase: perpendiular	r=-0,181 p=0,377	r=0,538** p=0,005	r=-0,214 p=0,294
Chase: wolfpack	r=-0,136 p=0,506	r=0,407* p=0,039	r=-0,168 p=0,412
Chase: Overall	r=-0,020 p=0,925	r=0,538** p=0,005	r=-0,220 p=0,280
Match: perpendicular	r=0,156 p=0,445	r=0,331 p=0,098	r=-0,176 p=0,391
Match: wolfpack	r=-0,052 p=0,802	r=0,380 p=0,056	r=0,032 p=0,878
Match: Overall	r=0,074 p=0,719	r=-0,312 p=0,121	r=-0,036 p=0,861

Table 2. Correlations between the different wolfpack tasks and the Corsi block-tapping task, Individualism and Collectivism. *: significant, with p<0.05; **: significant, with p<0.01.

DISCUSSION

In accordance with our hypothesis, we found that the Hong Kong group scored higher in the working memory tasks. We also found cultural differences in working memory after threat prime, in accordance with our hypothesis. However, no cultural difference in holistic or analytic perception, as measured by perceived animacy, was found.

Furthermore, we hypothesized that Hong Kong would score higher on collectivism, and Portugal would score higher on Individualism. While we found that Hong Kong scored higher on collectivism than Portugal, but we found no difference for Individualism. Moreover, the only subcategory of the AICS that showed a significant difference across cultures was "Harmony", which loads on collectivism. This suggests that the higher collectivism of the Hong Kong population, compared to the Portuguese population, is mainly due to increased levels of harmony, which is a measure of avoiding conflict (Shulruf et al., 2007) .Cluster analysis showed that for the Hong Kong population there were three main groups: the first scored high on collectivism and medium on individualism. For the second group, the reverse was the case. Finally, the last group scored high on both dimensions. This nicely explains how Hong Kong scored high on both individualism and collectivism. In contrast, the Portuguese population was lacking a group that scored high on collectivism and medium on individualism. But the group that scored high on individualism and medium on collectivism made up almost two thirds of the population. Unlike in the Hong Kong group, the remaining participants did not score high on both dimensions, but had midlevel scores. This explains why Portugal scored high on individualism but medium on collectivism. Our findings differ from those of Shulruf et al. (2011), who found that the largest group of Portuguese participants scored high

on collectivism and low in individualism.

While the individualism-collectivism distinction showed an effect between cultures, the distinction between holistic and analytic perception did not. We hypothesized that the Hong Kong group would be show more holistic perception and the Portuguese group would show more analytic perception, which could not be confirmed. That no cultural difference in the perception of the wolfpack effect was found may be in part explained by the fact that these cultures' differences in individualism and collectivism were not as profound as expected. Similarly, their level of holistic and analytic perception may also not differ as much. However, there was a main effect for the wolfpack and perpendicular condition. Participants from both cultures found it easier to identify that no chase was present in the perpendicular trials, than to identify that a chase was present in the wolfpack trials. Yet when we added individualism score as a co-variable, this effect disappeared. Furthermore, individualism score in the Portuguese group correlated stronger with chase perception in the perpendicular condition than in the wolfpack condition. This could mean that individualism, but not collectivism, is linked to the perception of this effect. It is intriguing that individualism correlated with chase perception in the Portuguese group only, and not in the Hong Kong group, even though differences in individualism across cultures were not significant. This may be related to the fact that almost two thirds of Portuguese participants scored high in individualism and medium in collectivism, while the Hong Kong group did not have a single large group with such striking differences in score. Ultimately, whether individualism is linked to perceived animacy is beyond the scope of this research. The low number of participants in each cluster also restricts interpretation of these effects. Further research with a larger sample would be needed to investigate this.

While cultures did not differ on the perception of the threat prime, the high percentage of correct responses indicates that participants did indeed perceive the wolfpack effect. One of our hypotheses was that working memory performances would differ across cultures in response to a threat prime. This seemed to be the case. The performance of the Hong Kong group stayed constant after a threat prime, compared to a neutral prime. In contrast, the performance of the Portuguese group declined after a threat prime. Thus the Hong Kong group showed better working memory performance after threat prime. The Hong Kong group also performed better than the Portuguese group over both conditions of this task. Similarly, the Hong Kong group was better at the Corsi block-tapping task, although this effect was only marginally significant. The findings on the working memory tasks are ultimately not strong enough to confirm out hypothesis that the Hong Kong group scores higher than the Portuguese group in working memory tasks.

Overall, these findings show that the differences between Hong Kong and Portugal are not as straightforward as assumed. Hong Kong's high level of Individualism prevents a categorization that puts the East Asian population at one end and the Western population at the other end of the Collectivism – Individualism spectrum. Rather, Hong Kong scores high on both individualism and collectivism, while Portugal scores high on only individualism. Other studies have found similar results that did not fit the individualism-collectivism distinction. For example, Kim et al. (2010) found that Koreans and Americans were equally collectivistic and

equally individualistic. In a different study, Oishi, et al. (2005) found that Americans and Japanese did not differ on Individualism, and Americans scored higher on collectivism than Japanese. These findings reinforce the notion of Oyserman et al. (2002) that an individualism-collectivism distinction should not be applied by default to all Western and East Asian cultures. More recently, other fields of research have also challenged the validity of the individualism – collectivism distinction (e.g. Brewer & Venaik, 2011). Considering the distinction between analytic and holistic perception, we may have been unable to discern effects across cultures because the chase perception task showed a ceiling effect (see figure 4). This task may have been too easy to meaningfully identify differences across cultures. It may be the case that everyone, regardless of their degree of analytic or holistic perception, scores high on this task due to a lack of difficulty. In retrospect, a direct measure of holistic and analytic thinking and perception would have been useful, such as the Analysis-Holism Scale developed by Choi, Koo and Choi (2007). Furthermore, the link between high holistic thinking and a high perception of animacy, while plausible, has not been empirically investigated in this experiment. Future research should try to validate the proposed differences in holistic and analytic perception between Hong Kong and Portugal, as well as the connection between holism and perceived animacy in the wolfpack task.

Therefore, in this study we do not know how analytic or holistic perception comes to bear on the effect a threat prime has on working memory. Whether Individualism or Collectivism has an effect on this also remains disputable. Both groups scored high on Individualism, but only Hong Kong scored high on Collectivism. This makes it tempting to suggest that collectivism is somehow involved in performing well after a threat prime. However, we found no correlation between collectivism score and chase perception in either condition, or between collectivism and performance on the match / no match task. This opposes such an interpretation. Future research on this subject may be warranted in order to see whether collectivism scores influence working memory performance in threatening situations. Similarly, whether individualism is linked to chase perception remains elusive and further research may prove insightful.

Strangely, the match / no match task did not correlate with the Corsi block-tapping task. This could mean that these tasks measured different aspects of working memory. Indeed, the Corsi block-tapping task is sequential, consisting of a slowly increasing number of blocks that have to be remembered. In contrast, the match / no match task used here requires one to attend to the whole picture at once, without gradually building up working memory load. In order to tell if a picture is the same as the one just seen during the wolfpack animation, one needs to attend to the whole screen and remember the position of several wolves at once. A replication of this study with more closely related working memory tasks might provide insight into cultural differences in working memory.

Conclusion

In summary, the Hong Kong group showed better working memory performance than the Portuguese group. Contrary to our hypothesis, working memory performance did not increase after threat prime. Instead, the Hong Kong group's performance

stayed constant, while the Portuguese group's performance dropped after threat prime. Although this experiment proved unable to show differences in analytic or holistic perception across cultures, differences were found in collectivism, with Hong Kong scoring higher than Portugal. However, no differences in individualism were found. This study shows that caution is advised when categorizing Western societies as individualistic and East Asian societies as collectivist. Furthermore, this study adds to existing knowledge by showing that working memory is differently affected by threat primes in these cultures.

Acknowledgements

This paper focused on working memory issues. In order to get a full understanding of all the different facets of this experiment, the reader is advised to also read Sachistal & Van der Lugt (In preparation), which focuses on the social psychological issues measured by the approach-avoidance task.
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MELLONEY WIJENBERG

A systematic review of the effects of early onset cognitive rehabilitation on acquired brain injury patients from a neural perspective

Review

Cognitive impairments – a frequent consequence of acquired brain injury (ABI) – are currently addressed by compensatory approaches within cognitive rehabilitation. However, several studies support a restorative approach, because a period of increased neural plasticity is seen in the first three months after ABI. Starting neuropsychological rehabilitation within this period could maximize functional improvement. To examine this hypothesis, a systematic review of randomized controlled trials on early onset cognitive rehabilitation programmes for ABI patients was executed. A total of thirty studies were included studying 1988 patients. Thirty-seven per cent was found to be effective in restoring (partly) multiple domains of cognitive functioning, especially visuospatial functioning and awareness. The influence of intervention onset on cognitive functioning was evaluated by comparing the effectiveness of early and late onset rehabilitation programmes. A new theoretical model, the Interplay Model, and guidelines for a more restorative approach in clinical practice and future research are discussed.
Keywords: Acquired Brain Injury (ABI), cognitive neuropsychological rehabilitation, systematic review, restorative approach.

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INTRODUCTION

Cognitive impairments are a frequent consequence of acquired brain injury (ABI). ABI can be subdivided in cerebrovascular accident (CVA) and traumatic brain injury (TBI). A CVA or stroke is the loss of brain function due to ischemia or haemorrhage (van den Berg & van Zandvoort, 2012). Ischemia, lack of blood flow, arises when a blood vessel is blocked while haemorrhage, loss of blood, arises due to a tear in the blood vessel. A CVA causes the loss of brain functionality which could comprise multiple cognitive functions. More than 50% of the CVA patients experience cognitive function disorders (Bots et al., 2009). Cognitive impairments can also be a consequence of TBI, which is brain damage due to an external force on the skull (Stapert & Spikman, 2012). The prevalence of ABI, especially CVA, is high and will increase enormously over the following decades due to the aging population and lower mortality rates (Koek et al., 2005). Which cognitive impairments are commonly seen after ABI are dependent on the locus and severity of the brain damage.

Commonly seen affected cognitive functions are attention (e.g. loss of ability to concentrate), memory (mostly anterograde), mental speed (e.g. slowness), social cognition (e.g. loss of empathy), executive functions (e.g. inability to plan, be cognitively flexible and regulate behaviour) and language (e.g. inability to speak). Cognitive rehabilitation tries to address these impairments and their enormous interferences with daily life activities and participation in society.

According to many national clinical guidelines cognitive rehabilitation is a standard component of rehabilitation programmes for ABI patients (van Heugten et al., 2012). The effectiveness of different cognitive rehabilitation programmes is well established by Cicerone et al. (2000, 2005, 2011). Especially, attention training after TBI and language and visuospatial training for respectively aphasia and neglect syndromes after stroke are found to be effective. Another conclusion by Cicerone et al. (2000, 2005, 2011) is that the current approach of cognitive rehabilitation is mostly compensatory, meaning that the patient is taught to compensate for their impaired functions with their intact functions (e.g. an agenda for memory problems). According Krakauer et al. (2012) this is a consequence of the proven effectiveness of compensatory interventions on functional outcomes. However, improving the impaired function itself and therefore minimalizing the interference with daily life activities would be a tremendous improvement for the patient, the patient's surroundings and the therapist.

Lately a new view towards neural plasticity of the adult brain has been extensively investigated in animal studies, which supports the possibility of improving impaired cognitive functions due to ABI. Neural plasticity is the possibility of neurons to structurally and functionally adapt.

In animal models it is found that after acquired brain injury heightened plasticity occurs in the residual neural circuits. This means that there is a higher possibility that other intact neurons could replace the damaged neurons and take over their original function and therefore restore the cognitive functioning of the patient. This plasticity is found on the level of cortical activation maps, neurotransmission, dendritic spine structures and axonal connections.

Dijkhuizen et al. (2003) found that cortical sensory maps are highly plastic within the first two weeks after a stroke. Directly after a stroke, unilateral sensory stimulation leads to activation of the ipsilateral cortex instead of the contralateral cortex. However, after two weeks the same sensory stimulation leads to activation of the contralateral cortex. The shift of an abnormal activity response to a normal activity response is correlated with level of sensory recovery. On a cellular level, Clarkson et al. (2010) found that in the first weeks after a stroke motor neurons are hypo-excitable due to diminished re-uptake of the inhibitory neurotransmitter GABA. This diminished re-uptake leads to more GABA in the synaptic cleft, which leads to less signal transduction. Fortunately, the excitability of the motor neurons is restored within two weeks and remaps limb functioning. Formation of new axonal connections, also known as axonal sprouting, and reorganization of dendritic spines, also known as dendritic spine morphogenesis, accompany this process (Brown et al., 2009).

An extensive amount of research has shown that the neurophysiological processes causing the plasticity in a human brain are comparable to the described neurophysiological changes in a rodent brain (Grossman et al., 2002; Sadato et al., 1996). This is highly influenced by the common role of the brain-derived neurotropic factor (BDNF) in rodents and humans. BDNF enables the structural changes needed for plasticity (Murphy & Corbett, 2009).

This heightened plasticity is the underlying mechanism for relearning the impaired function driven by brain injury and learning in the intact brain driven by behavioural experiences (Kleim, 2011; Krakauer et al., 2012). In the intact brain the amount of plasticity is negatively related to age, meaning that plasticity is very high in the immature brain and gradually diminishes after maturing (Eriksson et al., 1998). A short window of increased plasticity is seen in the first three months after acquired brain injury to provide rearrangement of impaired functions to different intact brain regions by several structural changes. This is the so-called intrinsic repair/learn capacity of the brain (Krakauer et al., 2012).

There is a possibility that rehabilitation enhances this intrinsic repair capacity of the brain, so that there is interplay between the two causal factors of neuroplasticity: injury and experience. In other words, rehabilitation could optimize the neural plasticity and therefore the functional improvement. Importantly, in the phase of heightened plasticity, the first four weeks after ABI in rodents and the first three months after ABI in humans, the brain can maximally recover and maximal functional improvement can take place (Kleim et al., 2008; Krakauer et al., 2012; Murphy & Corbett, 2009). Biernaskie et al. (2004) reported that rats exposed to rehabilitation initiated within the period of heightened plasticity (5 days after stroke) experienced a significantly greater recovery than rats exposed to rehabilitation which was not initiated within the period of heightened plasticity (30 days after stroke). This finding and comparable findings by Chikahisa et al. (2006) and Kim et al. (2006) support the possibility that rehabilitation enhances this intrinsic repair capacity of the brain. However, implementing rehabilitation or training in the first days, could have the opposite effect, namely worsening of the impairment, due to overuse effects (Kleim et al., 2008; Krakauer et al., 2012; Murphy & Corbett, 2009).

Translating these findings to humans and clinical practice would imply to start interventions for cognitive impairments within these three months, because these interventions could benefit from the restorative ability of the brain. So, if heightened neural plasticity is a requirement for maximal effectiveness of cognitive rehabilitation, which implies a more restorative approach, this should be shown in a greater effect of early onset cognitive rehabilitation on cognitive functions than late onset cognitive rehabilitation measured by the same outcome measures.

To examine the possibility and evidence for this restorative approach in a clinical setting, randomized controlled trials evaluating the effectiveness of cognitive rehabilitation programmes for ABI patients, starting within three months after the injury will be reviewed. Content and effects of these programmes will be evaluated. Furthermore, a comparison between early onset cognitive rehabilitation programmes and late onset cognitive rehabilitation programmes is made. Implications for clinical settings and future research are discussed according the Interplay Model.

METHODS

The following method was used to identify randomized controlled trials (RCTs) evaluating early onset interventions targeted at cognitive impairments as a consequence of acquired brain injury, published within the period from January 1970 until August 2010.

The database created by van Heugten et al. (2012) was filtered by an eight exclusion criterion concerning early onset interventions, because their systematic literature search identified randomized controlled trials (RCT's) evaluating both early onset and late onset interventions targeted at cognitive impairments as a consequence of acquired brain injury, published within the period from January 1970 until August 2010.

The systematic literature search, which was executed by van Heugten et al. (2012), used PubMed and PsycINFO and was based on the articles found by Cicerone et al. (2000, 2005). For an overview of the search terms, see table 1. This process yielded 1963 published articles in PubMed and 959 in PsycINFO. In total 2832 articles were found after exclusion of duplicates.

Studies were only included if they addressed the effect of a cognitive rehabilitation programme in a randomized controlled trial with a non-progressive human adult ABI sample, which was defined operationally in the search terms. Only randomized controlled trials were included because of their high validity.

Further study selection was done on the basis of the following seven exclusion criteria: (1) no intervention; (2) other design than RCT; (3) reports without explicit description of randomization of patients; (4) subjects did not have acquired brain injury; (5) pharmacological interventions; (6) aim of intervention was not cognitive impairments; (7) language was not English. An article could be excluded based on title, abstract or full paper.

As already mentioned, for the purpose of this article an eight exclusion criteria

was needed, namely that the intervention started later than three months after acquired brain injury (time since injury was longer than 91 days).

All included RCTs were identified by extracting the early onset interventions from the database created by van Heugten et al. (2012). Their database included 95 articles of which 30 articles started their intervention within three months after acquired brain injury. These 30 articles were included. See figure 1 for an overview of the selection process.

After study selection the articles were assigned to categories according to their primary area of intervention as was done in the previous reviews of van Heugten et al. (2012) and Cicerone et al. (2000, 2005, 2011): awareness, visuospatial functioning, memory, attention, executive functioning, apraxia, language and communication and multi-domain studies. The investigated domains of the selected 30 studies were awareness, visuospatial functioning, attention and language and communication. The following data was extracted: (1) intervention characteristics (duration, intensity, form); (2) patient characteristics (number of patients, type of injury, time since injury); (3) treatment outcome; (4) content of effective treatment.

Table 1. Search terms used for the period from January 1970 till August 2010 (van Heugten et al., 2012)

	Search Terms
Cognitive domain	Attention/concentration, information processing/slowness, awareness/ insight, cognition, communication, executive/planning/organisation/ regulation, language/aphasia, memory, perception/perceptual/agnosia/ neglect/visual, problem solving, reasoning, apraxia/dyspraxia
Rehabilitation	Rehabilitation, remediation, education, training, retraining, paging system, treatment, treatments, therapy
Acquired brain injury	Stroke, brain injuries/brain-injuries/brain injury/brain-injury/brain injured/ brain-injured, head injuries/head-injuries/head injury/head-injury/ head injured/head-injured, brain damage/brain damaged, tbi/head trauma/traumatic, cerebrovascular disorders/cerebrovascular accident/ cerebrovascular accidents/cva/stroke/poststroke/post-stroke/post stroke, chronic aphasia

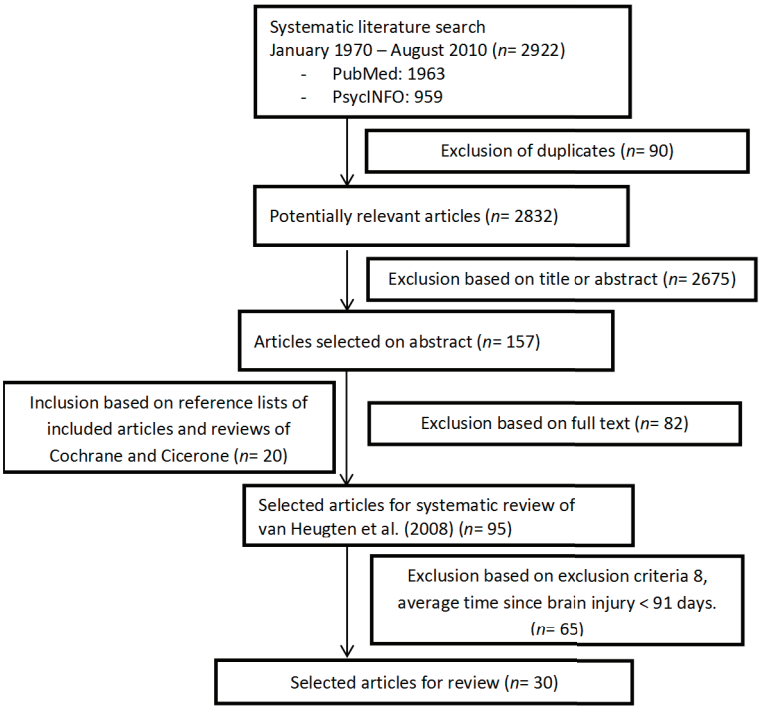

Figure 1. Flow-chart

RESULTS

The frequency of studies per domain (including all references) is shown in table 2. Most studies were conducted in the area of visuospatial functioning (n= 16). This is in line with the extensive amount of neglect rehabilitation research, which contains one of the oldest rehabilitation RCTs, namely the RCT conducted by Weinberg et al. (1977).

Table 2. Study Domains

Domain	n	%	Author, year of publishing
Awareness	5	17	Carter et al., 1983 Salazar et al., 2000 Sarkamo et al., 2008 Soderback, 1988 Vanderploeg et al., 2008
Visuospatial Functioning	16	53	Antonucci et al., 1995 Cherney et al., 2003 Edmans et al., 2000 Fanthome et al., 1995 Kalra et al., 1997 Katz et al., 2005 Lincoln et al., 1985 Luukkainen et al., 2009 Rossi et al., 1990 Rusconi et al., 2002 Si Hyun et al., 2009 Taylor et al., 1971 Tsang et al., 2009 Weinberg et al., 1977 Weinberg et al., 1979 Wiart et al., 1997
Memory			
Attention	4	13	Barker-Collo et al., 2009 Malec et al., 1984 Mazer et al., 2003 Novack et al., 1996
Executive Functioning			
Apraxia			
Language and communication	5	17	Bakheit et al., 2007 David et al., 1982 Lincoln et al., 1984 Wertz et al., 1981 Wertz et al., 1986
Multi-domain			
Total	30	100	

Treatment characteristics.

Type of therapy was not reported in seven studies. The other 23 studies provided individual therapy.

Frequency, duration and intensity were not always described in the original papers, for this reason the following data is based on 24 studies which did report these treatment characteristics. Frequency, duration and intensity are summarized in table 3. On average patients received 4.0 hours therapy per week for 8.7 weeks.

Table 3. Frequency, duration and intensity

	Mean	Standard Deviation
Hours	40.0	70.8
Week	8.7	9.1
Hours/Week	4.0	2.6

Patient characteristics.

In the included 30 studies 1988 patients were studied. The mean (SD) number of patients per study was 70.3 (66.3) ranging from 4 to 360. The largest study by Vanderploeg et al. (2008), for instance, included 360 adult veterans or active duty military service members with moderate to severe traumatic brain injury. Eight studies have included a sample of 20 participants or less, indicating a small sample size, which could influence interpretation of results.

The mean age of the patients was 59.9 years (SD = 13.9), ranging from 25.5 to 77.0. Most of the studies which included younger subjects assessed traumatic brain injury patients, while most of the studies which included older subjects assessed CVA patients.

The time since the acquired brain injury was described in all studies, which was also necessary for inclusion in this review. The intervention started on average 44.1 days after the injury (*SD* = 24.4, with a minimum of 4.7 days and a maximum of 88.3 days).

The most studied diagnosis was stroke, which was studied in 23 articles (76.7%). Other studied diagnoses were traumatic brain injury (*n*= 5, 16.7%) or heterogeneous populations (*n*= 2, 6.7%).

Treatment Outcome.

In 11 of the 30 studies the experimental treatment was found to be beneficial (*n*= 11; 36.7%), meaning that the improvements in the impaired cognitive functions were significantly higher in the treatment group compared to the control group. These improvements were measured by various outcome measures, like the line bisection task and letter cancellation test for visuospatial functioning. The other 19 studies concluded with no differences between experimental and control treatment (*n*= 13; 43.3%) or ambiguous results (*n*= 6; 20.0%). Ambiguous results consisted primarily of various effects on different domains.

Content of effective early onset interventions.

An overview of the characteristics of the included studies which examined effective early onset interventions can be found in table 4. Sample size, time since injury, content of interventions, outcome measures and results are mentioned.

Table 4. Characteristics of included RCTs which examined effective early onset interventions.

Domain	Study	N tot	N exp	N cntrl	Diag-nosis	Time since injury (days)	Intervention Experimental group	Intervention Control group	Mean hours a week (weeks)	Results	P
Visuospatial functioning	Antonucci et al., 1995	20	10	10	Stroke	79	Neglect rehabilitation training, which consisted of visuo-scanning training, reading and copying training, copying of line drawings on a matrix and giving a description of a figure.	General cognitive stimulation.	Exp: 5 (8) Control: 3 (8)	The experimental group showed significantly greater improvement on standard neglect tests, like the letter cancellation test, compared to the control group. These improvements were generalizable to daily life activities as measured by the Functional Scale for the Evaluation of Neglect.	<0.05
	Kalra et al., 1997 Full text unavailable	47	24	23	Stroke	6	Spatial-motor cueing based intervention with emphasis on restoration of functioning.	Conventional therapy, which concentrated on movement pattern, motor activity and restoration of tone.	Exp: 2.8 (12) Control: 3.3 (12)	- The experimental condition significantly outperformed the control condition on the letter cancellation subtest. Due to the movements of the affected limb, summation of brain activation will arise which will cause improvements in attentional skills and spatial exploration. - The experimental group stayed significantly shorter at the hospital than the control group.	0.01 0.001
	Katz et al., 2005	19	11	8	Stroke	41	Virtual reality based street crossing training.	Computer based visual scanning tasks.	Exp: 9 (4) Control: 9 (4)	- During virtual street crossing the experimental group made significantly fewer accidents than the control group. - The experimental group looked more to the left during virtual street crossing than the control group.	<0.04 NS

Weinberg et al., 1977 Full text unavailable	57	25	32	Stroke	70	Visual training (VT) + occupational therapy.	Occupational therapy, but no visual training (VT).	Exp: VT 5 (4) Control: VT 0 (4)	After one month the experimental group significantly outperformed the control group on different specific scanning tasks (e.g. letter cancellation task) and academic reading tasks which were hypothesized to depend on intact visual scanning.	<0.05
Weinberg et al., 1979 Full text unavailable	53	30	23	Stroke	42	Visuo-perceptual remediation with emphasis on sensory awareness and spatial organization.	Standard rehabilitation.	Exp: 5 (4) Control: 5 (4)	After one month the treatment group showed a significant greater improvement on visuospatial and academic tasks than the control group, which was most apparent in subjects with more severe perceptual impairments.	<0.05
Wiart et al., 1997	22	11	11	Stroke	33	The Bon Saint Come method (BSC), during which the patient wears a thoraco-lumbar vest with a metal pointer above his head in order to point to targets, while receiving visual and auditory feedback. In addition the patient received additional physiotherapy (PT) and occupational therapy (OT).	Standard rehabilitation.	Exp: BSC 5 (4) PT 10 (4) OT 1 (4) Control: 17 (4)	Scores on the assessments of neglect (e.g. line bisection) and ADL function (activities of daily living), measured by the Functional Independence Measure (FIM), showed a significant higher improvement in the experimental group than in the control group.	<0.05

Language & Communication	Wertz et al., 1986 Full text unavailable	121	A: 43 B: 38	40	Stroke	36	A: First twelve weeks stimulus-response treatment by speech pathologist in clinic (SP), then twelve weeks no treatment (NT). B: First twelve weeks stimulus-response treatment by trained volunteers at home (VOL), then twelve weeks no treatment (NT).	First twelve weeks no treatment (NT), then twelve weeks stimulus-response treatment by speech pathologist in clinic (SP).	ExpA: SP 9 (12) NT 0 (12) ExpB: VOL 9 (12) NT 0 (12) Control: NT 0 (12) SP 9 (12)	After twelve weeks the two treatment groups performed comparable and significantly better than the control group on communicative ability measured with various language tests.	<0.05
Attention	Barker-Collo et al., 2009	78	38	40	Stroke	19	Standard care + Attention Process Training (APT).	Standard Care.	Exp: APT 5 (4) Control: APT 0 (4)	After five weeks the experimental group outperformed the control group as measured by the Integrated Visual Auditory Continuous Performance Test (IVA-CPT) indicating that APT had a significant positive effect on attention	0.01
Awareness	Carter, Howard & O'Neil, 1983	33	16	17	Stroke	5	Conventional therapy + cognitive skill remediation training. This training involved numerous elements, like paper and pencil tasks, positive reinforcement and immediate feedback.	Conventional therapy.	Exp: 1.5 (3) Control: 0 (3)	The treatment group showed a significantly higher improvement than the control group within three skill areas: visual scanning, visual-spatial orientation and line judgment measured by exercises of the Thinking Skills Workbook.	0.00

Sarkamo et al., 2008	55	A: 19 B: 19	17	Stroke	9	A: The music group listened for two months every day to music + standard rehabilitation. B: The language group listened for two months every day to audio books + standard rehabilitation.	Standard rehabilitation.	ExpA: 11.2 (8) ExpB: 9.1 (8) Control: 0 (8)	- After three months verbal memory, measured by the story recall subtest of the RBMT, improved significantly more in the music group than in the other groups. - After six months focused attention recovery, measured by summed reaction times during the Stroop task, was significantly higher in the music group than in the other groups.	<0.05 <0.02
Soderback, 1988. Full text unavailable	67	A: 15 B: 19 C: 15	18	Stroke	68	A: Intellectual function Training (IFT) plus standard rehabilitation. B: Intellectual Housework Training (IHT) plus standard rehabilitation. C: IFT + IHT + standard rehabilitation.	Standard rehabilitation.	ExpA: 3 (12) ExpB: 3 (12) ExpC: 2 (16) Control: 0 (11)	The three experimental groups were significantly more effective on intellectual functioning than the control group, measured by the Intellectual Function Assessment (IFA) and the Intellectual Housework Assessment (IHA).	<0.05

*Effect sizes are not mentioned because they were not reported or unavailable to the author.

DISCUSSION

Several studies showed the existence of a time window of heightened plasticity in the first three months after acquired brain injury (Kleim et al., 2008; Krakauer et al., 2012; Murphy & Corbett, 2009). Due to this finding it was hypothesized that early onset interventions would be more effective in enhancing cognitive functioning of ABI patients compared to late onset interventions, by benefiting from this intrinsic neural repair capacity. In order to examine this hypothesis, early onset interventions (time since injury <3 months) targeted at cognitive impairments as a consequence of acquired brain injuries (ABI) were identified by performing a systematic literature search. It is important to note that identification of some RCTs may have failed, although the used strategy identified those found in other systematic reviews (Bowen & Lincoln, 2008; Greener et al., 2008).

Thirty randomized controlled trials have been identified of which eleven found beneficial effects for stroke patients. Out of these eleven studies six studies were primarily aimed at treating spatial neglect and therefore improving visuospatial functions. More research on TBI patients is needed to generalize these results to TBI patients.

To investigate the cause of the effectiveness of the eleven studies and provide guidelines for clinical practice and research, therapy elements that the effective treatments have in common were identified per domain. In order to identify common therapy elements, content of the treatment programmes and hypothesized underlying mechanism were evaluated.

Extraction of communal treatment elements in the 'Visuospatial functioning' domain leads to the two conclusions. Firstly, Wiart et al. (1997) and Karla et al. (1997) assessed an effective training for spatial neglect which both comprises motor activation. A possible theory for this effectiveness could be that motor activation leads to a change in brain activity in networks which are linked with networks controlling visuospatial functioning. Through this indirect route, the increased activation will draw awareness to the neglected contra-lateral visual field and therefore, treating spatial neglect. However, this conclusion should be interpreted with caution. These findings are based on a relatively small sample size and assume a similar effect of brain activity and localization on this activity, which may not be valid. Secondly, Antonucci et al. (1995) and Weinberg et al. (1977, 1979) have shown that visual scanning training and other forms of visual trainings are a beneficial addition to standard rehabilitation for neglect patients. However, it remains unclear if the improvements on the specific tasks also generalize to the daily live activities of these patients. Katz et al. (2005) did show that virtual reality training could be beneficial for neglect patients and that these effects generalize to daily life activities. However, the programme should be further developed before application in clinical practice and future research is needed for replication of these results and further investigation of the causes of the effectiveness of these interventions. Overall, it

can be concluded that the addition of motor training or visual scanning training is beneficial for treating neglect patients in the early stage of recovery. Motor training is often already part of the rehabilitation programme because of motor impairments. Further research into motor rehabilitation programmes with a 'side'-effect on cognitive impairments is necessary, while this could be a very effective, cost and time efficient standard rehabilitation programme for stroke patients.

Extraction of communal treatment elements in the 'Awareness' domain leads to the conclusion that awareness could be improved significantly in stroke patients by intensive training as an addition to the standard cognitive rehabilitation programmes. The discussed studies examined three different kinds of training, but all required an active role of the patient, which could be (part of) the reason for the effectiveness. Translation of these findings to traumatic brain injury patients should be studied more extensively, since these discussed studies included only stroke patients.

Extraction of communal treatment elements is not possible for the domain 'Language & Communication' and 'Attention', because there is only one effective study within these domains.

Another possible reason for the effectiveness of the eleven studies could be the interplay between cognitive rehabilitation and the heightened neural plasticity during the first three months after ABI (Chikahisa et al., 2006; Kim et al., 2006; Kleim, 2011; Sarkamo et al., 2008). If this neural plasticity is indeed a requirement for maximal effectiveness of cognitive rehabilitation, this should be shown in greater effect of early onset cognitive rehabilitation on cognitive functions than late onset cognitive rehabilitation measured by the same outcome measures.

To examine if the onset of the intervention has an influence on its effectiveness the results of early onset rehabilitation programmes (intervention onset < 3 months) were compared with the results of effectiveness of late onset rehabilitation programmes (intervention onset > 3 months), acquired by filtering the database of van Heugten et al. (2012). The proportion of studies that found a positive effect in cognitive functioning is higher in the late onset rehabilitation programmes than in the early onset rehabilitation programmes. Regarding late onset rehabilitation, more than half of the studies, 42 out of the 64 studies (65%), found beneficial effects of the intervention. Regarding early onset rehabilitation, only 11 out of 30 studies (36.7%) found beneficial effects of the intervention. These findings suggest that starting earlier with the rehabilitation programme does not increase the beneficial influence of the programme on improving cognitive functions due to ABI.

However, this conclusion should be carefully interpreted, because this is a rough comparison. The homogeneity of groups is restricted due to the difference in the distribution of the amount of studies in all the different domains and the difference in participant characteristics (only stroke patients vs. mixed patients) and outcome measures.

More importantly, the characteristics of the interventions differ between the early onset group and the late onset group. In the early onset group, interventions are primarily aimed at restoring the cognitive function. However, in the late onset group, interventions are primarily aimed at compensating for the cognitive impairment with intact cognitive functions. When the same outcome measures are

used, measuring cognitive functioning, the same level of improvement could be found between the two groups. However, in the early onset group this could be the consequence of actual improvement of the cognitive function, while in the late onset group this could be the consequence of the compensating behaviour. For example, when a patient has memory impairments, due to early onset interventions the actual memory function will improve and therefore the patient reports less forgetting. In contrast, due to late onset interventions the patient learns to compensate for his memory loss by using a pager and therefore the patients reports less forgetting. The outcome is the same, but the underlying mechanism is different and therefore limits comparability.

The above mentioned reasons made clear why comparison between these two groups, early onset rehabilitation programmes and late onset rehabilitation programmes, is invalid. Therefore, no direct conclusions about the effect of onset on the effectiveness of cognitive rehabilitation can be made based on this comparison.

However, Antonucci et al. (2008) executed a RCT with onset of intervention as independent variable to examine if onset of rehabilitation had an effect. There were two groups of stroke patients, one group received the neglect rehabilitation training immediately after admission to the clinic and the other one received the same training after two months. They found that both groups obtained similar improvement which implies that the moment of onset of intervention had no influence on the effectiveness, which is in accordance with the results of this review.

Controversially, Horn et al. (2005) and Salter et al. (2005) reported in their reviews, which included 830 and 435 post stroke patients respectively, that earlier initiation of rehabilitation is preferred for stroke patients. For instance, Salter et al. (2005) reported that interventions started within 30 days result in greater functional gains than interventions started beyond 30 days. This means that there is a significant difference in functional outcome between interventions started within one month after brain injury and interventions started more than one month after injury. Yet, there are no differences in functional outcomes between interventions started one month after brain injury and interventions started two or more months after brain injury. This implies that a functional improvement window of one month appears after a stroke. Applying this to the results of Antonucci et al. (2008), the conclusion that the moment of onset of intervention has no influence on the effectiveness is invalid, since it is based on the comparison of interventions both started beyond 30 days, namely 79 days. These results imply that the hypothesized critical period of the first three months after brain injury seems to be too liberal and should be restricted to only the first month, which also limit interpretation of the current results of the review because the liberal 3 months criteria for early onset interventions was used.

Combining the discussed neural findings and clinical findings, a new theoretical model is suggested, named the Interplay model. This model states that maximal effect of a rehabilitation programme on cognitive impairments due to ABI can be achieved by initiating the intervention within the first month instead of the hypothesized three months. The first month forms the so-called window of opportunities, where the amount of neural plasticity exceeds the threshold for interplay between neural plasticity and rehabilitation. Furthermore, the model states

that neural plasticity is enhanced in the first three months after brain injury, but that this enhancement gradually decreases after the first month till the premorbid level of neural plasticity is reached after three months. According to Wade et al. (1985) a similar course of recovery is seen in motor functioning of stroke patients. So only within the first month, the amount of neural plasticity is high enough for the possibility that rehabilitation enhances the intrinsic repair capacity of the brain, so that there is interplay between the two causal factors of neuroplasticity: injury and experience. In other words, only when a rehabilitation programme is implemented during a specific time window, where neural plasticity is above a certain level, it will cause a significantly greater effect on cognitive impairments than implemented beyond this time window. This model states that there is an effect of onset on the effectiveness of cognitive rehabilitation. So to maximize the effect of a rehabilitation programme on cognitive impairments due to ABI, the intervention should be initiated within the first month, the so-called window of opportunities. However, as mentioned before, implementing rehabilitation or training in the first days, could have the opposite effects due to overuse effects. This is included in the model, since the amount of neural plasticity does not exceed the threshold for interplay during the first week (Kleim et al., 2008; Krakauer et al., 2012; Murphy & Corbett, 2009). See figure 2 for a clarification of this model.

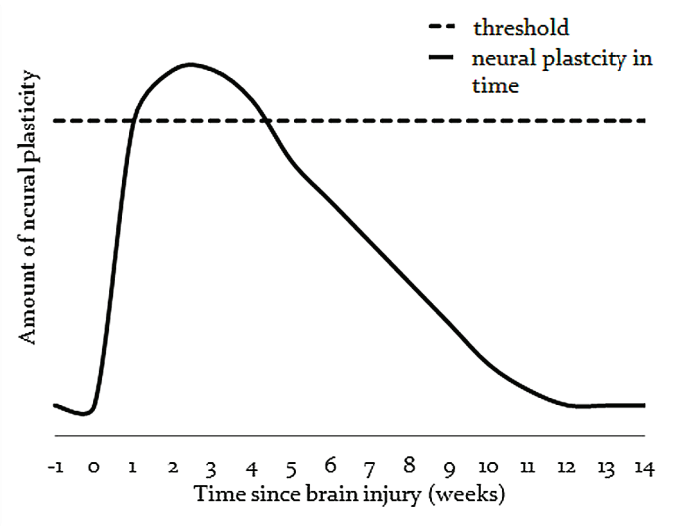

Figure 2. The Interplay Model. The black line displays the time course of the amount of neural plasticity, based on discussed neural findings from human and animal studies. Zero on the X-axis represents the moment of injury. The dotted line displays the hypothesized threshold for interplay between neural plasticity and rehabilitation. In the time window where neural plasticity exceeds this threshold, effect of the cognitive intervention will be maximized, the so-called window of opportunities. Note that there is always neural plasticity, but that this neural plasticity is increased during the first 12 weeks and only exceeds the threshold between one and four weeks after brain injury.

Future research is needed to validate the accuracy and application of this model. This research could consist of multiple randomized controlled trials on cognitive rehabilitation for ABI patients with onset of intervention as independent variable. So ideally, two randomly formed groups consisting of ABI patients receive the same intervention aimed at restoration of the cognitive function, but initiate at different moments regarding their time since injury. The interplay model suggests that the early onset group should start their intervention after one week and the late onset group after more than one month.

Moreover, limitations of the Interplay Model are that the time course of neural plasticity is primarily based on animal studies. More research is needed to investigate the generalizability of the findings of neural plasticity in rodents to the human brain. Furthermore, the findings supporting the existence of a time window of interplay were solely based on stroke patients. Therefore, more research validating translation of these findings to other acquired brain injuries is needed due to their difference in type of injury. TBI is most often diffuse, whereas brain injuries due to stroke are most often local.

Despite these limitations, the Interplay Model is in line with the findings of all discussed studies and the results of the discussed systematic review. Therefore, the main implications for clinical practice are to shift from a compensatory approach to a restorative approach, where treatment of cognitive impairments should already start in the first month after ABI. This is even earlier than the current view of early cognitive rehabilitation of the first three months suggests. So, it is important to start within this first month with cognitive rehabilitation in order to utilize the natural brain recovery mechanism of heightened plasticity and therefore maximize the possibility of restoration of the impaired cognitive function. Compensatory approaches can always be offered, their effectiveness is, unlike the restorative approach, not dependent of a level of neural plasticity exceeding the interplay threshold. So ABI patients should receive earlier rehabilitation than the current standard compensatory rehabilitation, namely within the first month after brain injury, the window of opportunities. Use it or lose it.

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LISA WILBERS

The effect of testing on the vulnerability to misinformation in adolescents and adults

Review

False memories are a frequently recurring problem in the courtroom and therefore research on this topic is highly needed. In the present study, 51 adolescents and 50 adults were tested to investigate the effect of testing on the vulnerability to misinformation. The main expectation was that these groups have different levels of susceptibility to misinformation. Using the Fuzzy Trace Theory as a framework, it was hypothesized that the testing effect influences these different levels of susceptibility to misinformation. On the first testing day, after viewing a video of a theft, participants received gist or verbatim questions. On day two, an eyewitness statement, manipulated with misleading information, was presented, after which participants received a final memory test on a verbatim level. It was found that (i) susceptibility to misinformation decreases with age and therefore adolescents were more vulnerable to misinformation than adults and (ii) the testing effect only applied when no misinformation was presented. Limitations might be that participants received forced choice questions and that there was no free recall, which occurs in real-life situations as police interviews.
Keywords: False memory, Fuzzy Trace Theory, Testing effect, Misinformation, Adolescents

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INTRODUCTION

A false memory is a recollection of events or experiences which is distorted or fabricated, and did not actually happen (Loftus, 1980). In general, there are two forms of false memories: spontaneous false memories and implanted false memories (Reyna, 1995). Spontaneous false memories arise endogenously due to cognitive distortions (Reyna & Brainerd, 1998). On the other hand, implanted false memories result from exogenous misinformation. Misinformation after exposure to an event can affect the memory of that event and also memory reporting of details of that particular event.

Loftus, Miller, and Burns (1978) introduced the so-called misinformation paradigm, which now is commonly used in studies where susceptibility of eyewitnesses to misleading post-event information is being investigated. Research suggests that participants are more prone to suggestion if misinformation and misleading suggestions are reported in a memory test, compared to a control condition with no misinformation and misleading suggestions (Loftus, 1978). Regardless of whether post-event information is misleading or consistent, this information is integrated into the event memory of a witness, which is called the misinformation effect (Loftus, 1978).

The storage of event memory can be explained by the *Fuzzy-trace theory* (FTT). The FTT states that individuals who witness an event will derive two independent memory traces or representations of event details – verbatim and gist traces (Brainerd, Reyna & Ceci, 2008; Rivers, Reyna, & Mills, 2008). Verbatim representations store exact surface details of an event or experience (i.e., exact words and details of a story), whereas gist representations consist of meaning-based memory for the event or experience (i.e., the theme of a story) (Howe, Wimmer, Gagnon, & Plumpton, 2009). Gist representations are superior to verbatim representations in memorability and accessibility (Brainerd & Reyna, 2001). More precise, gist processing is a favored retrieval mode over time and at immediate memory testing (Pansky & Koriat, 2004).

A study by Bouwmeester and Verkoeijen (2011) suggests that gist traces strengthen even more when a memory test is conducted. The effect that taking a memory test improves retrieval of information is called the *testing effect* (Roediger, Jacoby & McDermott, 1996; Roediger & Karpicke, 2006a; Roediger & Karpicke 2006b). The relation between the testing effect and the FTT is explained by the theory that the gist traces will strengthen because these traces are used to reconstruct and retrieve information from participants' memory (Bouwmeester and Verkoeijen, 2011). On the other hand, a study phase followed by a restudy phase will strengthen verbatim traces. In line with this argumentation, it is demonstrated that repetition and restudying can lead to a decrease of false memories due to the strengthened verbatim traces (Brainerd, Payne, Wright, & Reyna, 2003). The main question underlying the study of Pansky and Tenenboim (2011) is whether testing

can serve as a buffer for the susceptibility to misleading post-event information. They conclude that strengthened event memory on the verbatim level can inoculate against misinformation. On the other hand strengthening gist level memories did not decrease the effect of misinformation.

The testing effect can have both a beneficial (Warren & Lane, 1995), and a detrimental (Chan, Thomas, & Bulevich, 2009; Chan & Langley, 2011) influence on suggestibility to misinformation. Research has shown that when a test is preceded by misleading post-event information, the misinformation effect increases (Chan, Thomas & Bulevich, 2009). More precisely, although the testing effect enhances memory of a witnessed event, retrieval practice can increase people's suggestibility to manipulated information. This means that even though it has consistently been shown that correct recall improves by repeated testing, this testing could have a reversed effect when misinformation is introduced.

The effect of misinformation on children is a recurrent point of discussion in the legal field. However, little research is available on this effect on adolescents. The current study focuses on the effect of misinformation in this age group. Still, it is important to consider children as a comparison group (Brackmann, in prep.). Recent research has shown that false memories increase between early childhood and young adulthood under certain circumstances (e.g., Brainerd, 2013; Ceci & Bruck, 1993). Brainerd (2013) states that the risk to develop false memories increases drastically with age. Therefore, it is no longer justifiable to use the assumption that children's testimonies, compared to adults' testimonies, should in general be more infected with false memories. With regard to the developmental reversal it is important to note that this phenomenon only exists when adults have higher knowledge of meaning connections than children (Sutherland & Hayne, 2001).

In the present study adolescents and adults were tested to investigate the effect of testing in combination with misinformation on false memories. It is a well-established finding that children's memory relies less on gist representation compared to adults, and therefore children are expected to be less vulnerable to the production of false memories (Reyna & Kiernan, 1994). It can be expected that memory processes and therefore production of false memories works differently in adolescents, than in adults. Decision-making (i.e., the cognitive process that results in the selection of a course of action out of alternatives) in adolescents is more intuitive and less computational compared to adults (Rivers, Reyna & Mills, 2008). Adolescents find themselves between relying on verbatim analysis and relying on gist-based intuition (Reyna & Brainerd, 1995). In this study, the focus is on adolescents as nearly no study on this subject has been conducted that takes this age group into account (Jack, Leov, & Zajac, 2014). The research question is therefore: to what extent does testing have an effect on adolescents' vulnerability to misinformation compared to adults?

It was hypothesized that (i) adolescents will be less vulnerable to misinformation compared to the adult sample in this study, due to less reliance on gist representation; (ii) according to the testing effect, performance should be improved on the items of the final memory test, that were tested (Roediger, & Karpicke, 2006); and (iii) that the misinformation effect is expected to manifest itself in an impaired performance on items with misinformation in the final memory test, compared to items with no misinformation in the misinformation account.

METHOD

Participants

In total there were 101 participants (45 male participants), which is a subsample of the participants in the study of Brackmann (in prep.). 51 adolescents (M=15.04, SD=.52, age range from 13.69 to 16.59) and 50 adults with (M=22.32, SD=1.99, age range from 18.91 to 27.33) were tested. The different age groups were adjusted in order to make the different stages of development easy distinguishable. The verbatim condition included 26 adolescents and 27 adults, and the gist condition 24 adolescents and 24 adults. Participants were recruited from secondary schools in the surroundings of Maastricht (The Netherlands), and Maastricht University. Adults were compensated for participation by receiving either one subject point or an Iris Cheque with a value of €7.50. The adolescent participants were tested at their secondary schools during class time. The adult group was tested in a lab at Maastricht University. Informed consents were obtained from students, and from parents or legal guardians, in case of under-age participants. In both age groups the division of participants in the gist-testing or verbatim-testing group was counterbalanced.

Materials and procedure

Participants were tested individually on two consecutive days. On both days, test sessions lasted about fifteen minutes. At the start of each session, participants were told to concentrate and pay close attention as at the end of the session questions would be asked about the video. The first day, participants were presented with a video about an electrician entering a house to do chores and repair a list of electrical objects (see Takarangi, Parker, & Garry (2006) for a detailed description of the stimulus film). After a nonverbal filler task of approximately 3 minutes, the interpolated cued-recall task was presented to the participants. This task consisted of eight items with two questions each, one general question and one group specific question which was either gist- or verbatim-based.

After a 24-hour time interval, on day 2, participants received an audio version of an eyewitness account about the video which they viewed on day 1. In this eyewitness statement eight items were manipulated with misleading information (see Table 1). Four of these items were tested earlier in the interpolated cued-recall task on day 1 and four items were not tested earlier. Afterwards there was a nonverbal filler task that served as a pause between the eyewitness account and the cued recall task. The cued recall task consisted of 18 questions on the verbatim level about the video of Eric the Electrician. Besides the eight misinformation items, this final memory task included items that were not manipulated in the eyewitness account which were either neutral or verbatim. Neutral items were mentioned in the eyewitness account on a basic level and verbatim items were mentioned on a more detailed level. The questions in this cued recall task were presented in the same order for every participant, but were previously randomized by Takarangi et

al. (2006). Lastly, the participant was asked not to tell details of the study to their classmates or other students until the study had finished and thanked for his or her participation.

It should be noted that in this particular study a forced-choice report was applied, which implies that participants cannot choose the level at which they report their memories. All questions were accompanied by two possible answers, which participants had to choose from. Both these cases of forced choice could have an effect on participants' performance and therefore they should be taken into account when analyzing the data (Payne, Elie, Blackwell and Neuschatz, 1996).

Table 1. Misinformation items in the cued-recall task on day 2.

Correct item displayed in the video on day 1	Misinformation item in the eyewitness account on day 2	Testing condition in interpolated cued-recall task on day 1
Magazine Time	Magazine Newsweek	Tested
Photo of the Tower of Pisa	Photo of the Eiffel Tower	Untested
Made bed	Unmade bed	Tested
Black cap	Blue cap	Untested
RJ's Electrician	AJ's Electrician	Untested
Wristwatch	Wall clock	Untested
White cup	Yellow cup	Tested
Coca-Cola	Pepsi	Tested

Design

Two age groups were compared: adolescents and adults. Age was considered as a between subjects factor. Participants engaged in an interpolated cued-recall task where half of the participants in each age group received questions on the gist level, and the other half received questions on the verbatim level. A between subjects comparison was made between gist representations and verbatim representations. A within subjects design was used to compare the influence of misinformation or no misinformation and the effect of tested and untested items on memory of participants in the final memory test. The within subject items of the final memory test consisted of four levels: tested misinformation x tested no misinformation x untested misinformation x untested no misinformation. The dependent variable of this study was the correct or incorrect answers participants gave on the final memory test. Concluding, this resulted in a 2 (age: 14-15, adults) x 2 (testing group: gist testing, verbatim testing) x 2 (testing condition: tested, untested) x 2 (misinformation condition: misinformation, no misinformation) mixed model design, with age and testing group as between-subject factors and testing and misinformation condition as within-subject factors.

Results

As in this study, both a between subjects design and a within subjects design were used, the collected data were analyzed with the use of a four-way mixed-model ANOVA. The between-subjects factors were represented by the interpolated-testing mode and age. The within-subjects factor was the misinformation condition and the test-condition. This resulted in a 2 (age: 14-15, adults) x 2 (testing group: gist testing, verbatim testing) x 2 (testing condition: tested, untested) x 2 (misinformation condition: misinformation, no misinformation) mixed model design.

First, the responses of participants on the final memory test were compared by a function of age group, testing group, testing condition and misinformation condition. Table 2 presents the proportion of incorrect answers on the final memory test in each age group and condition. These data are used for the following analyses with a four-way mixed-model ANOVA.

A significant main effect of testing condition was found, $F(1, 204) = 72.489$, $p < .001$, $\eta^2 = .262$ indicating an effect of tested versus untested items on performance on the final memory test. There was also a significant main effect of misinformation condition, $F(1, 204) = 251.465$, $p < .001$, $\eta^2 = .552$. Participants displayed impaired performance on items with misinformation in the eyewitness account compared to items with no misinformation.

Table 2. Mean (M) and standard deviation (SD) of the proportion of incorrect answers on the final memory test as a function of age, testing group, testing condition and misinformation condition.

Testing group	Testing condition	Misinformation condition	Age			
			14 – 15 years old		Adults	
			M	SD	M	SD
Gist	Tested	Misinformation	.47	.32	.20	.22
		No misinformation	.03	.08	.05	.12
	Untested	Misinformation	.53	.20	.26	.23
		No misinformation	.24	.20	.23	.20
Verbatim	Tested	Misinformation	.41	.28	.20	.18
		No misinformation	.04	.08	.07	.11
	Untested	Misinformation	.38	.20	.36	.20
		No misinformation	.25	.18	.18	.16

An interaction effect was found between the factors misinformation condition and age group, $F(3, 204) = 7{,}870$, $p < .001$, $\eta^2 = .104$. This indicated that the influence of misinformation in the eyewitness account on performance in the final memory test differs per age group. It was found that the effect of misinformation decreased with age, as illustrated in figure 1. Thus, performance on the final memory test of adolescents (14 to 15 years old) was more influenced by misinformation in the eyewitness account, compared to performance of adults (figure 1). The mean misinformation effect (y-axis) was higher as performance on the final memory test decreased. Analyzing the simple effects, it was indicated that within both age groups misinformation had a significant effect. When comparing age group 14 to 15 year-olds ($F(1, 208) = 85.86$, $p < .001$, $\eta^2 = .219$) with adults ($F(1, 208) = 14.89$, $p < .001$, $\eta^2 = .038$) it could be concluded that adolescents were more influenced by the misinformation in the eyewitness account.

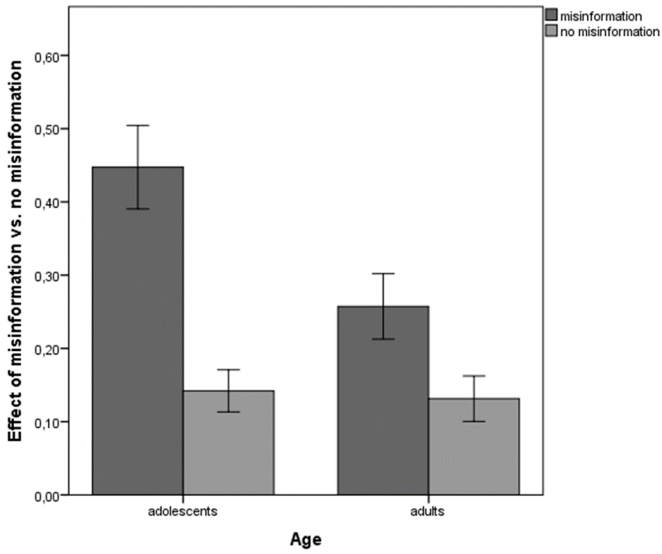

Figure 1. The effect of misinformation compared to no misinformation per age group on the proportion of incorrect answers on the final memory test. The effect of misinformation was significant (p < .001) in both age groups. Error bars: 95% CI.

There was also an interaction effect for testing condition (tested vs. untested items) and misinformation condition (misinformation vs. no-misinformation items), $F(1, 204) = 27.682$, $p < .001$, $\eta^2 = .119$. This effect of within subject manipulation showed that the misinformation in the eyewitness account influenced the effect of testing on performance on the final memory test (see also figure 2). The simple main effects show that when an item consists of misinformation, no testing effect is found in the performance on the final memory test ($F(1, 207) = 3.04$), $p = .083$, $\eta^2 = .014$). In other words, there was no significant effect for testing and misinformation. But when no misinformation was applied, an effect of testing was found ($F(1, 207) = 130.32$, $p < .001$, $\eta^2 = .380$). Thus, the testing effect was only present when there was no misinformation presented in the eyewitness account.

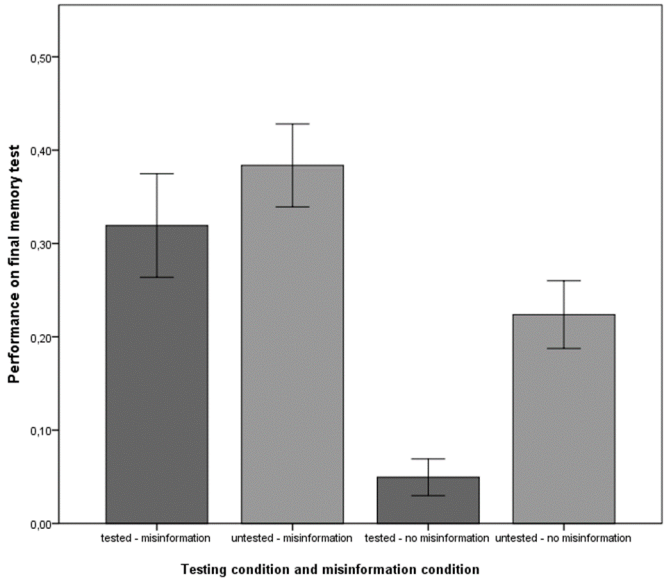

Figure 2. The effect of testing and misinformation on performance on the final memory test. A higher level of performance on the test means more errors. A significant effect of testing was only found on items with no misinformation, when misinformation was presented no testing effect was found. Errors bars: 95% CI.

DISCUSSION

The aim of this study was to examine the influence of the testing effect on the vulnerability to misinformation in adolescents and adults. Emphasis was put on adolescents as most studies have focused on children and adults. It was hypothesized, in line with FTT (Rivers, Reyna, & Mills, 2008), that adolescents are more vulnerable to misinformation than adults. The vulnerability of different age groups depends on the paradigm being used in a study. Children are more prone to suggestive information, while adults are more prone to spontaneous false memories (Otgaar, 2013).

The current study shows that adolescent participants are more susceptible to misinformation than adults. When misinformation was introduced both groups showed impaired performance, although adolescents' performance on the final memory test was more impaired than the performance of the adults. The study of Brackmann (in prep.), which is related to the present study, showed that children are more susceptible to misinformation than adults. Those findings are in controversy with the recent developmental reversal, but it should be noted that a developmental reversal is only present when adults have higher knowledge of meaning connections than children. This assumption could be an explanation for the increased effect of misinformation in children (Brackmann, in prep) and in adolescents, in this study,

compared to adults. When combining the results of both studies, it is indicated that adolescents can be located between children and adults on a continuum of susceptibility to misinformation. Further research could focus on including a greater extent of age groups, which should give a more complete picture on the distribution of different age groups with respect to susceptibility to misinformation.

Another important finding of this study is that, when age is held constant, the testing effect is dependent on the misinformation condition. It shows that an effect of interpolated testing on performance on a memory test only exists when no misinformation is presented. It is remarkable that when misinformation is presented, no testing effect is observed. This implies that the testing effect does not occur when someone is influenced by misinformation. In relation to this it can also be stated that, regardless of the testing effect, participants' performance on the final memory test was negatively influenced by misinformation as the error rate increased with the application of misinformation.

As the FTT states that the suggestibility to misinformation increases when relying more on gist representations compared to verbatim representations (Rivers, Reyna & Mills, 2008), an interaction between misinformation and testing group was expected. However, no support for this hypothesis was found in the present study. The interaction effect of testing group and misinformation did not appear to have an influence. It was expected that the difference between gist and verbatim testing on the first day would influence the performance on the final memory test after the misleading post-event information. This can also be linked to age, because children rely less on gist representations compared to adults and are therefore, in line with the developmental reversal, considered to be less suggestible to false memories (e.g., Brainerd, Reyna, & Ceci, 2008; Reyna & Kiernan, 1994). Although the FTT sets out that children rely less on gist representations, the results of the overarching study (Brackmann, in prep.) point out that children are more vulnerable to the misinformation effect. It is therefore assumed that the hypothesized effect of gist and verbatim testing on the vulnerability to misinformation might not apply.

A limitation of the current study is that participants were forced to report their answers on either gist or verbatim level. In real-life situations, such as a police interview, respondents have the option to choose the level on which they report information (Payne, Elie, Blackwell, & Neuschatz, 1996). As discussed by Payne et al. (1996) the forced-choice answer format could affect the performance on a memory test, because a forced-choice report could lead to an increased proportion of errors. In addition to the fact that participants were divided into separate conditions of report, they were prompted to choose one of the two answer options that accompanied the questions. The absence of the possibility for free-recall of memories could have influenced participants' performance, or at least might differentiate participants' performance from performance in an interview setting.

The conclusion of this study is that susceptibility to misinformation increases with age, and adolescents are more susceptible to misinformation than adults. Furthermore, the testing effect only applied when there was no misinformation. When misinformation comes into play, the testing effect cannot be found. A suggestion for additional research is to more extensively examine the relation between misinformation and testing. By including an adolescent age group, this

study raises an important area of development in the research on false memories, as there is only limited research on this age group. It is important to expand studies on the effect of misinformation on adolescents.

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