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### Victimization in psychosis

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# **CHAPTER 8**

## General Discussion

The overarching aim of this dissertation was to investigate victimization in psychosis. Individuals diagnosed with a psychotic spectrum disorder are prone to become the victim of a crime and of other forms of aggression. For this patient group victimization prevalence rates are four to six times as high as in the general public (de Vries et al., 2018a). Studies on patients with a psychotic disorder have revealed a large impact of victimization, leading to for example substance abuse, depression (Fisher et al., 2017), more severe symptomatology and poorer illness outcome (Newman et al., 2010). Because of the increased risk of victimization and its large impact, an intervention specifically targeted at victimization is vital for this population. Therefore, we have developed a body-oriented resilience therapy with elements of kickboxing; BEATVIC. The therapy aims to prevent victimization by addressing putative risk factors which are potentially modifiable through an intervention, such as social cognition, assertiveness, self-esteem, self-stigma, aggression regulation and illness insight. To target these factors, a body-oriented approach was combined with elements of social cognition training, assertiveness training and martial arts. In this dissertation we explored the feasibility of BEATVIC by means of a pilot and subsequently we performed a multicenter randomized controlled trial to investigate effects on behavioral outcomes (e.g. incidents of victimization, associated factors and generic outcomes such as quality of life and recovery). In addition, we conducted an MRI study to gain more insight into the putatively underlying neural basis, which could shed light on implicated mechanisms. More specifically, we investigated which brain areas or networks related to social cognitive processes are associated with victimization of individuals with psychosis, and explored the effects of the intervention on brain activation. Because the therapy contains physical exercise we also reviewed studies which have investigated the neural effects of physical exercise interventions in people with a psychotic disorder and healthy individuals. In the following paragraphs, important findings will be summarized and integrated. Next, I will share some general considerations connected to this work. Subsequently, clinical implications and directions for future studies will be indicated and finally, I will end with a number of concluding remarks.

### **SUMMARY AND INTEGRATION OF FINDINGS**

#### **Feasibility of BEATVIC**

In preparation of the large randomized controlled trial to investigate the effectiveness of BEATVIC described in Chapter 3 and Chapter 4 we performed a feasibility study in **Chapter 2**. The aim of this study was threefold: a) to explore the feasibility of the intervention, b) to improve the therapy protocol and c) to explore suitable outcome measures for a subsequent RCT.

It took approximately two months, and 155 invitations to patients to include 24 participants with a psychotic disorder from five in- and outpatient facilities of the psychosis department of GGZ Drenthe in Assen, the Netherlands. This indicates that therapists were interested and willing to refer their patients, and that a substantial number of patients were inclined to participate in the therapy and the

study. Furthermore, the mean attendance was 85.3% and 88% of the participants attended fifteen or more of the twenty weekly sessions. These attendance rates are high compared to other group interventions for patients with a psychotic disorder in which 50% of the participants attended 2/3 of sessions (Beebe et al., 2009) and 22.9% attended at least half of the sessions (McGuire et al., 2013).

Based on evaluations by participants, the body-oriented therapist, the experiential expert, the kickboxing expert and the researchers that developed the intervention, we applied several adaptations to the therapy protocol for the subsequent RCT. Multiple repetitions of important themes and techniques were added to the protocol, more challenging exercises (e.g. high kick, sparring) were incorporated, an intensive workout on kickboxing pads at the end of each session was included into the protocol and time for discussion was reserved. In all, the frequency, duration and structure of the therapy were considered appropriate.

According to the participants the therapy had a positive effect on identifying and setting boundaries, recognizing those of others, self-esteem, faith in own strength, confidence, recognizing dangerous situations, feelings of safety, and patients thought they had a lower chance of becoming a victim. Some participants noticed that they had lost weight and improved their endurance. To measure endurance and physical activity objectively we included a modified shuttle test and use of pedometers to the RCT. Furthermore, the explored outcome measures (IVM, CTS2, NAS-PI, STAXI and ISS) were considered suitable as participants were well able to understand them and assessors were able to apply them.

Overall, BEATVIC was found to be a feasible therapy for people with a psychotic disorder. Small adjustments were made to the therapy protocol. Participants subjectively had the idea that BEATVIC had a positive effect on (risk factors of) victimization.

### Subsequent study design

Based on the findings of the feasibility study in Chapter 2 we designed a multi-center randomized controlled trial. We describe the research protocol of this study in **Chapter 3**. Six mental health care institutions in the Netherlands participated in the study. Patients were randomly assigned to either BEATVIC or Befriending. BEATVIC consists of twenty weekly group sessions of 75 minutes led by a therapist trained in body and movement oriented interventions (in the European literature called a psychomotor therapist, see [www.psychomot.org/](http://www.psychomot.org/)) and an expert by experience. All BEATVIC trainers received a train-the-trainer course consisting of four sessions of 2,5 h during which most important exercises were trained and the most important background was discussed. When a BEATVIC group started, the study investigators and body-oriented therapist of the training team monthly visited a session in order to monitor the training and to supervise the onsite trainers. Similarly, the organizers of the befriending sessions were trained by the study investigators and were monthly supervised. Befriending consists of 20 social contact sessions in which participants

can socially interact with each other in an informal setting. Individual befriending has been used as a control treatment in several RCTs examining CBT for psychosis and has been proven a credible and acceptable control condition with regard to expectancy, enjoyment and therapy drop-out (Bendall et al., 2006). We chose to use an active control group in order to eliminate the effects of common intervention factors such as weekly social contact in a group. Based on a sample size calculation 48 participants per condition were required to find a medium effects size on our outcome measures with an alpha of 0.05 and a power of 0.80. Considering a drop-out of 25%, we aimed to include a total of 120 participants in our trial.

Before, directly after (post), six months after (follow-up I), eighteen months after (follow-up II) and 30 months after (follow-up III) the intervention period patients complete an assessment conducted by independent blind assessors measuring risk factors of victimization, victimization incidents and generic outcomes (e.g. recovery, quality of life). In the short term we were primarily interested in risk factors of victimization as these were direct targets of the therapy. At follow-up we were mainly interested in actual victimization incidents: as these incidents do not occur often, it was expected that a change would be best detectable over a longer period of time. Secondary outcomes were generic outcomes such as quality of life, recovery, social functioning, trauma symptoms, physical activity and fitness.

We added an MRI sub study in which we acquired both functional and structural scans to investigate underlying factors of victimization and of effects following BEATVIC. Of the total study sample of 120 participants we aimed to include 44 participants in this MRI sub study. Before and directly after (post) the intervention period participants were scanned while they performed two face processing tasks. We chose to use a task with brief presentation (600 ms) of individual angry, fearful and neutral faces to investigate quick implicit threat response. Previous studies examining implicit threat response in participants with a psychotic disorder also used angry and fearful face expressions (Kumari et al., 2011; Mason et al., 2016). While angry expressions signal a direct and immediate threat from a potential perpetrator, fearful expressions indicate a possible presence of a significant source of threat in the environment, as witnessed by others (Fridlund, 1994). To retain their attention on the task, participants had to indicate whether a presented face was male or female. In addition to an implicit task including brief individual face stimuli, we applied the Wall of faces task that contains a group of predominantly angry faces or predominantly happy faces presented for 2000 ms. Participants explicitly have to indicate whether they detected more angry or happy faces. At baseline we aimed to investigate neural correlates of angry face processing in relation to victimization, at post assessment we were interested in effects of BEATVIC on brain regions involved in emotional processing since this was a target of the treatment. This dissertation concerns assessments before, directly after and 6 months after the intervention period.

### **Behavioral results of BEATVIC**

The effects of BEATVIC on risk factors, victimization incidents and general outcomes are presented in **Chapter 4**. While our study protocol in Chapter 3 specified a desired inclusion of 120 participants, a total of 105 participants were included which resulted in a lower power than anticipated. These participants were allocated to one of eighteen treatment groups (nine BEATVIC, nine befriending). Of the initial 105 participants, 77% completed the post-assessment and 70% participated in the follow-up I assessment. Study drop-out rates are similar to respectively those of other non-pharmacological (20%; (Szymczynska et al., 2017)) and pharmacological studies (30%; (Leucht et al., 2014) including individuals with a psychotic disorder. With regard to therapy drop-out, 28% of the 53 participants discontinued BEATVIC and 40% out of 52 participants discontinued Befriending. Especially for befriending these rates were higher than expected based on previous studies (Bendall et al., 2006).

Intention-to-treat multilevel analyses revealed no differences between the BEATVIC group and the befriending group directly after and six months after the intervention period on our outcome measures. Sensitivity analyses with participants that had participated  $\geq 75\%$  of the sessions revealed similar results. While participants in the feasibility study had indicated that BEATVIC may have a positive effect on risk factors and the chance of victimization by means of subjective questions, based on validated questionnaires in the RCT no effects following BEATVIC were found. These findings are in contrast with for example studies reporting positive effects of physical exercise interventions on self-esteem, self-efficacy, social skills, positive and negative symptoms and physical outcomes in people with a psychotic disorder (Holley et al., 2011; Malchow et al., 2013; Scheewe et al., 2013). With regard to victimization, de Waal et al. (2018) reported at least a 50% reduction in the number of past-year victimization incidents at 14-month follow-up after a group training focused on enhancing emotion regulation skills, conflict resolution skills and street skills compared to care as usual. However, future analyses on our second and third follow-up assessment have to reveal whether BEATVIC has an effect on victimization in the long term. Although this particular study does not provide evidence for BEATVIC as an effective therapy, it may be too early to draw definite conclusions and disregard the approach altogether, which may be premature. In the General considerations section we will elaborate on possible explanations for these null findings.

### **Neural correlates of victimization**

In **Chapter 5** baseline results of the MRI substudy were described. Because emotional face processing has been suggested to be associated with victimization in this patient group (Baas et al., 2008; DePrince, 2005b), a group of victimized participants ( $n=19$ ) and a group of non-victimized participants ( $n=20$ ) underwent MRI scanning, during which they viewed angry and neutral facial expressions. While GLM analysis and gPPI analysis yielded no differences in respectively brain activation and brain connectivity in response to angry faces between a group of victimized and a group of non-victimized participants, ICA revealed more deactivation of the sensorimotor network in victimized patients.

The lack of GLM and gPPI findings are in contrast with studies reporting differential brain activation to facial expressions between traumatized and non-traumatized groups (Cisler et al., 2014; Crozier et al., 2014; Garrett et al., 2012). However, although victimization may be considered as a form of trauma, these studies included participants with subsequent PTSD symptoms indicating a large impact on their mental wellbeing, which may have resulted in a more severely disabled sample in comparison to our participant sample. Furthermore, groups sizes in our study were rather small, considering the heterogeneous nature of the sample with regard to illness duration and illness severity.

In comparison to GLM and gPPI analyses, ICA analysis, which enables identification of networks in a data-driven manner, is more sensitive to detect subtle differences between participants (Koch et al., 2009). Decreased activation in sensorimotor regions and decreased connectivity within the sensorimotor network has been associated previously with the common symptom ‘freezing of gait’ in patients with Parkinson’s disease, which refers to a brief abortion of movement (Mi et al., 2017; Shine et al., 2013). Deactivation of the sensorimotor network in victimized participants may resemble to some extent the freeze response reported in traumatized individuals in response to threat (Hagenaars et al., 2012; Roelofs et al., 2010). Freezing is a common type of defense behavior alongside fight and flight that occurs in response to (the anticipation of) threat and is considered to play a role in threat-related disorders such as PTSD (Hagenaars et al., 2008; Rizvi et al., 2008). Indeed, Hagenaars et al. (2012) found stronger freezing reactions to aversive IAPS pictures in previously traumatized individuals compared to people who had never experienced an aversive life event (e.g. sexual or physical assault, serious accidents).

In summary, compared to non-victimized participants with a psychotic disorder, patients with a history of recent victimization show more deactivation of the sensorimotor network in response to angry faces. This finding indicates a freezing response previously observed in traumatized individuals in response to threat (Hagenaars et al., 2012; Roelofs et al., 2002). Since the sensorimotor network is associated with victimization, changes in this network should be investigated following BEATVIC, which aims to prevent (re)victimization.

### Neural effects of exercise interventions

As physical exercise is a key component of BEATVIC, it was considered worthwhile to perform a systematic review on the neural effects of physical exercise interventions in psychotic disorder and in healthy individuals in **Chapter 6**. Although a large body of research has revealed positive effects of physical exercise on behavioral, cognitive and physical outcomes (Dauwan et al., 2016; Firth et al., 2015) and emerging evidence shows meaningful neural effects (Firth et al., 2018), a systematic search yielded only nine studies concerning psychotic disorders and six studies on healthy individuals. We found that the majority of studies focused on hippocampal volume or functioning, reporting beneficial effects of physical exercise. In addition, in psychosis increased

extrastriate body area (EBA) activation (Takahashi et al., 2012) and increased white matter fiber integrity in tracts relevant to the disorder were found (Svatkova et al., 2015). In healthy individuals decreased connectivity of the dorsolateral prefrontal cortex (DLPFC) indicating greater cognitive efficiency was reported (Tao et al., 2017). Comparing individuals with a schizophrenia spectrum disorder and healthy individuals, most studies found similar effects for both groups although the effect in schizophrenia spectrum disorders may be attenuated which is in line with previous literature on brain plasticity (Reif et al., 2006b; Schmitt et al., 2015).

Overall we found beneficial neural effects of exercise interventions, although results seem inconsistent across studies due to differences between the included studies. As a result of limitations of the studies we formulated several suggestions and directions for future research at the end of Chapter 6. Three of these suggestions were directly relevant for our subsequent study on neural effects of BEATVIC: 1) an average weekly exercise frequency of at least two times a week and a duration of at least twelve weeks might be the minimum to detect neural changes; 2) it is recommended to use a control condition in which participants receive the same amount of attention and face-to-face interaction to exclude a Hawthorne effect (Mccambridge et al. 2014); 3) future studies should expand their focus, by investigating neural mechanisms underlying positive effects of physical exercise on positive symptoms, negative symptoms and symptoms such as depression, social withdrawal and social cognition. Consequently, we did not expect changes in hippocampal volume following BEATVIC as the frequency of exercise was only once a week (1), we added befriending as an active control condition (2), and with regard to the last suggestion (3), instead of focusing on the hippocampus special emphasis was on the effect on neural mechanisms underlying emotional face processing (dimension of social cognition).

### Neural effects of BEATVIC

In **Chapter 7** we examined effects of BEATVIC on brain regions involved in emotional processing. This is of relevance, since emotional face processing has been suggested to be associated with victimization and social cognition in general is an important treatment target. While we were the first to investigate BEATVIC, several previous studies examined neural effects of social cognition training (SCT), which also targets social cognition and emotional face processing. Because earlier studies on SCT in psychosis reported increased activation of early visual processing areas, frontal areas, and facial expression recognition areas such as the insula and amygdala (Eack et al., 2010; Habel, Chechko, et al., 2010; Keshavan et al., 2011), it was hypothesized that BEATVIC would lead to increased activation in these areas as well. Furthermore, as we found stronger deactivation of the sensorimotor network during processing of angry faces in a victimized group of patients in Chapter 5, we additionally explored the effect of BEATVIC on the sensorimotor network. Based on the review of neural effects following exercise interventions in Chapter 6, we checked whether there was an effect on hippocampal volume (for reasons of comparison), although no effect was expected. Indeed, no differences in hippocampal volume nor gray matter and white matter

between the BEATVIC group (n=19) and the Befriending group (n=20) following the intervention period were found. Hence, brain volume was not included as a covariate in further analyses. GLM analyses also yielded no differences between groups over time. This may be partly explained by the small sample size. Most previous fMRI studies on social cognition training or brain stimulation interventions in psychosis included around 20 participants (Bais et al., 2017; Habel et al., 2010; Hooker et al., 2012; Luckhaus et al., 2013), which is still modest. In line with our hypotheses, ICA revealed increased activation of the salience network to threatening faces in BEATVIC compared to Befriending. A trend for increased activation of the (medial) visual network to (a group of predominantly) angry faces, and decreased deactivation in the sensorimotor network in response to fearful faces in BEATVIC was observed. Thus, while we found more deactivation of the sensorimotor network in a group of victimized patients in Chapter 5, BEATVIC resulted in a trend of decreased deactivation of this network. To aid interpretation of these findings, we propose that increased activation of the salience network and visual network may suggest more elaborate processing of visual information and/or an increased alertness for potentially dangerous faces. Decreased deactivation in the sensorimotor network might indicate a reduced tendency for “freezing” and enhanced action readiness in response to indirect threat. Further studies are needed to confirm these suggestions.

### GENERAL CONSIDERATIONS

When reflecting on findings in this dissertation it is important to consider choices and characteristics regarding the study design of the included studies. Key aspects that warrant discussion concern sample characteristics, outcome measures and direction of causality.

#### Sample characteristics

In the studies presented in this dissertation participants were not specifically selected based on risk factors of victimization. While in the intake assessment eligibility was evaluated based on study selection criteria, risk factors were not investigated because the patient group in general has a priori increased chances of victimization. Indeed in the feasibility study (Chapter 2) 75% of the participants had been victimized five years preceding assessment and 21% in year preceding assessment, in the RCT (Chapter 4) 57% had been victimized and in the MRI study (Chapter 5 and 7) roughly 48,7% had been the victim of personal crime five years preceding assessment. However, whereas in Chapter 5 (baseline MRI results) the non-victimized and victimized group of participants were evenly distributed enabling comparison between these groups, in Chapter 2 (feasibility study), Chapter 4 (RCT) and Chapter 7 (MRI post results) this may have resulted in a study sample also including participants that were not per se prone to victimization. For example, patients that already had high levels of self-esteem, assertiveness and empowerment and experienced no problems with social functioning. For a portion of the participants this might have led to a ceiling effect, in which few space was left to improve following an intervention. In addition, because

of exclusion criteria (e.g. severe psychotic symptoms, substance dependence, co-morbid neurological disorder, co-morbid personality disorder, estimated IQ <70 and pregnancy) the samples may have precluded the most severely ill patients. Moreover, participants were excluded in case of substance dependence or personality disorder, while these characteristics were found to play a role in victimization in patients with a psychotic disorder as well (de Vries et al., 2018a). However, we chose to exclude patients with these issues because they may hinder structural participation in groups. In forensic settings, such aggression regulation interventions are therefore sometimes offered individually (Davidson et al., 2019; Haddock et al., 2009; Ross et al., 2013). In addition, broader selection criteria might have led to more heterogeneous samples.

Indeed, heterogeneity of participants is another important topic for consideration regarding sample characteristics. What works in a certain way for one specific kind of patient, may lead to different outcomes for another individual. Opposite/contradictory effects in for instance different (subgroups of) participants might cancel each other out. The BEATVIC study samples for example include both rather sub-assertive individuals that experience difficulties standing up for themselves and more aggressive individuals that may evoke conflicts ultimately leading to victimization. In the MRI study (Chapter 5 and Chapter 7) these different types of participants may have responded differently to threatening faces. With regard to the feasibility study (Chapter 2) and RCT (Chapter 4), while the latter might show increased control over externalized anger (e.g. 'I keep my feelings under control') and control over internalized anger (e.g. 'I try to calm down'), the first type of participants may show decreased scores on these scales following BEATVIC. In a future study subgroup analyses may aid in unraveling whether and how BEATVIC affects different kinds of patients. In general, RCT designs, which are still considered the gold standard in studying treatment effect, are based on groups means. However, what is best for the 'mean' or 'average' patient, may not be best for specific patients. When it comes to treatment, the 'one size fits all' principle may not be the best approach (Dallery & Raiff, 2014). More homogeneous participant samples for example in terms of illness duration may provide more concise and accurate information on treatment effects for a particular narrow patient group. Another method to overcome this issue is by performing n=1 studies for example by means of the experience sampling method (ESM; Myin-Germeys et al., 2009; Verhagen et al., 2016).

### **Outcome measures**

In the studies presented in the first part of this dissertation, in which we aimed to investigate the effect of BEATVIC on behavioral outcomes, we mostly used self-report questionnaires. Once per six months participants attended a 2,5 hour assessment during which they completed a test battery. While participants subjectively indicated that BEATVIC had a positive effect on risk factors (e.g. positive effect on identifying and setting boundaries, recognizing those of others, self-esteem, faith in own strength, confidence, recognizing dangerous situations etc.). In the pilot, nor in the RCT improvements were observed on the questionnaires. Although most studies

investigating therapies use these kinds of measures, common criticism concerns the limited nature of questionnaires. For example, self-report measures require insight in one's own behavior; they may be subject of social desirability bias or biases related to timing (Hogenelst et al., 2015; Wright, 2005). Questionnaires, like many evaluation methods are completed after the occurrence of an event so participants may forget important issues resulting in recall bias. However, selected questionnaires were well considered and were proven reliable and valid.

In the second part of this dissertation we investigated neural correlates of victimization and assessed neural changes following BEATVIC using two emotional face processing tasks. The emotional faces task consisted of brief presentation (600 ms) of angry, neutral, fearful and happy facial expressions and was used to investigate a threat-response. The Wall of faces task contained trials with a 'wall' of 32 faces with either more angry or more happy faces, more male or female faces or an equal amount of both types of faces to examine processing of a group of threatening faces. While both tasks have been used previously (Fisher et al., 2014; Simmons et al., 2006) and such emotional face paradigms are often used, they may lack personal relevance and ecological validity (Hogenelst et al., 2015). An attempt to solve the latter may be to show pictures or video clips of actual groups of people in a certain context, or to apply Virtual Reality in the scanner.

### **Direction of causality**

BEATVIC was developed based on pre-defined associated factors of victimization derived from the literature. While according to a meta-analysis it seems evident that certain factors are risk factors that may increase chances of subsequent victimization (de Vries et al., 2018a), it is also plausible that several factors from the victimization model are consequences of victimization. The direction of causality presumably stands out most in our study on neural correlates of victimization (Chapter 5), in which brain response to threatening emotional faces were investigated. While aberrant emotional face processing may for example result in the inability to detect threat and act adequately accordingly, victimization itself might induce alterations in threatening emotional face processing. As we used a cross-sectional design in this substudy, the direction of the association remains to be further elucidated.

## **CLINICAL IMPLICATIONS**

Our findings on victimization prevalence in people with a psychotic disorder are in line with results from previous studies (de Vries et al., 2018b; Kamperman et al., 2014a) and emphasize the urgent need for an intervention. Victimization can have a large impact on people's lives, and may lead to for example substance abuse, depression (Fisher et al., 2017), self-stigma (Horsseelenberg et al., 2016), more severe symptomatology and poorer illness outcome (Newman et al., 2010). Furthermore, victimization is a form of trauma and may cause PTSD symptoms. Indeed, findings from our MRI study on neural correlates of victimization could be interpreted from this perspective: we observed more deactivation of the sensorimotor network,

which may be regarded to be consistent with a freezing response previously seen in individuals with PTSD symptoms. While there are effective evidence based trauma-focused therapies for people with a psychotic disorder (van den Berg et al., 2015) also leading to a reduction of revictimization (van den Berg et al., 2016), prevention of victimization in the first place is eligible above having to remediate the debilitating consequences. This dissertation further underlines the importance of a preventive intervention and considerations regarding our sample characteristics implicate that such an intervention should be offered primarily to individuals who are at risk based on risk factors of victimization.

In the feasibility study presented in Chapter 2 patients subjectively indicated that BEATVIC had a positive effect on identifying and setting boundaries, recognizing those of others, self-esteem, faith in own strength, confidence, recognizing dangerous situations, feelings of safety, and participants thought they had a lower chance of becoming a victim. Furthermore, our interpretation of a possible freezing response in Chapter 5 may imply that exercises focused on fight, flight and freeze reactions in BEATVIC may be valuable. Moreover, Chapter 7 on neural effects revealed that BEATVIC led to increased activation of the salience network and a trend for increased activation in the visual network and decreased deactivation of the sensorimotor network. These findings imply more elaborate processing of visual information and/or an increased alertness for potentially dangerous faces, and enhanced action readiness in response to indirect threat. However, in contrast to subjective experiences and neural findings, we found no effects of BEATVIC on validated questionnaires regarding (risk factors of) victimization, physical variables and more general outcomes. Study limitations discussed in the general considerations sections might play a role in the lack of findings. Although this dissertation does not provide evidence for BEATVIC as an effective therapy, the included studies do not allow for definite conclusions, and it may be worthwhile to perform further research.

Exercise interventions in general were found to have a positive neural effect in people with a psychotic disorder and healthy individuals in our systematic review presented in Chapter 6. Since exercise interventions have been proven effective, their importance should be emphasized in clinical practice by implementation in mental health care. Exercise interventions and body-oriented interventions have been recommended in the Dutch treatment guidelines for psychotic disorders (GGZrichtlijnen). However, it seems challenging to activate people with schizophrenia spectrum disorder. Many of the desirable outcomes of exercise, such as mood improvement, stress reduction and increased energy, are inversely related to the experienced barriers of depressed mood, stress and fatigue some patients cope with (Firth et al., 2016). Providing more help of professionals specialized in body- and movement oriented interventions like psychomotor therapists to identify and achieve exercise goals may enable patients to overcome psychological barriers, and maintain motivation towards regular physical activity.

### **DIRECTIONS FOR FUTURE RESEARCH**

Based on the considerations presented above, I formulated several recommendations for future studies. In terms of continuing our own research, the effect of BEATVIC on victimization incidents in the long term, at follow-up II and follow-up III, needs to be assessed as incidents do not occur quite frequently. Additionally, it seems valuable to elaborate on patient characteristics, exploring whether and how BEATVIC affects certain subgroups or types of patients by means of moderator and mediator analyses. It is recommended to perform sensitivity analyses on a more severely ill subgroup or on 'high risk' patients that have been victimized previously and score high on associated factors.

Another important recommendation regarding study samples concerns addition of a healthy control group, especially in MRI studies. Although there is clear evidence that individuals with a psychotic disorder have difficulties with facial expression recognition and processing without a healthy control group, it is not possible to determine whether the differences in activation between the victimized and non-victimized groups in Chapter 5 are specific to patients with psychosis. The same holds for the neural effect reported in Chapter 7: increased activation of the salience network and visual network might indicate that BEATVIC normalizes activation in the (medial) visual network and the salience network, however, to confirm this, a future study including a healthy control group is needed.

Furthermore, future studies are recommended to use more fine-grained and ecologically valid measures as opposed to rather general and inflexible questionnaires (Hogenelst et al., 2015). For example, ESM allows for frequently repeated sampling of affect, thoughts and experiences, with the purpose to investigate temporal dynamics and relationships in a naturalistic setting (Myin-Germeys et al., 2009). On a related note, for MRI studies it might be valuable to explore possibilities for more ecologically valid tasks for example by the use of Virtual Reality. In addition to its application of an outcome measure or diagnostic tool, VR also enables patients to experiment with behaviour and practise with skills in a more realistic setting. Therefore, VR seems very suitable to implement in an intervention targeted at victimization (Klein Tuente et al., 2018).

Finally, there is a great need for prospective longitudinal research to investigate the direction of causality between associated factors of victimization and the occurrence of victimization incidents. Particularly, building upon our cross-sectional study, future studies need to determine the (bi)directional relationship between threatening emotional face processing and victimization.

### **Concluding remarks**

In this dissertation we assessed the efficacy of a body-oriented resilience therapy aimed at preventing victimization of individuals with a psychotic disorder by targeting associated factors. Participants subjectively indicated a positive effect of BEATVIC on

identifying and setting boundaries, recognizing those of others, self-esteem, faith in own strength, confidence, recognizing dangerous situations and risk of victimization. Furthermore, findings of more deactivation in the sensorimotor network in victimized patients, possibly indicating a ‘freeze’ reaction in response to angry faces, imply that BEATVIC may be valuable as the intervention includes exercises focused on fight, flight and freeze reactions. Moreover, at the neural level, although no effects were found on the questionnaire measures, BEATVIC resulted in increased activity in the salience network and a trend for increased activation of the visual network and decreased deactivation in the sensorimotor network. These findings are in need of replication and thus caution is needed in interpreting them. They may indicate more elaborate processing of visual information and/or an increased alertness for potentially dangerous faces, and enhanced action readiness in response to indirect threat. Although this dissertation does not provide compelling evidence for BEATVIC as an effective therapy, the performed studies also do not allow the conclusion to disregard this approach. We consider it worthwhile to perform further research based on recommendations derived from methodological considerations regarding sample characteristics and outcome measures.

### **Text box 1.** Overview of main findings

#### ***Part I***

- BEATVIC is a feasible therapy: therapists are willing to refer their patients and patients are inclined to participate (Chapter 2).
- Patients subjectively indicate that BEATVIC has a positive effect on (associated factors of) victimization (Chapter 2).
- BEATVIC revealed no short term effects on associated factors of victimization as measured with validated questionnaires (Chapter 4).

#### ***Part II***

- Compared to a non-victimized group of patients with a psychotic disorder, a victimized group of patients showed more deactivation in the sensorimotor network to angry facial expressions indicating a ‘freeze’ response to threatening information (Chapter 5).
- Exercise interventions have a positive effect on hippocampal volume, activation and connectivity, extrastriate body area activation and white matter fiber integrity in patients with schizophrenia (Chapter 6).
- Neuroimaging studies on exercise interventions should expand their focus by investigating neural mechanisms underlying positive effects of physical exercise on behavioral outcomes (Chapter 6).
- Compared to Befriending, BEATVIC showed increased activation in the salience network and a trend for increased activation in the visual network and decreased deactivation of the sensorimotor network (Chapter 7).