# The resilience framework as a strategy to combat stress-related disorders

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ABSTRACT

Consistent failure over the past decades to reduce the high prevalence of stress-related disorders has motivated a search for alternative research strategies. Resilience refers to the phenomenon that many people maintain mental health despite exposure to psychological or physical adversity. Instead of aiming to understand the pathophysiology of stress-related disorders, resilience research focuses on protective mechanisms that shield people against the development of such disorders and tries to exploit its insights to improve treatment and, in particular, disease prevention. To fully harness the potential of resilience research, a critical appraisal of the current state of the art – in terms of basic concepts and key methods - is needed. We highlight challenges to resilience research and make concrete conceptual and methodological proposals to improve resilience research. Most importantly, we propose to focus research on the dynamic processes of successful adaptation to stressors, in prospective longitudinal studies.

MAIN TEXT

Each year, more than half a billion people around the globe suffer from a mental disorder such as anxiety, post-traumatic stress disorder (PTSD), depression, or addiction that can to some extent be traced back to the influence of exogenous or endogenous stressors. Such stressors include traumatic events, challenging life circumstances or life transitions, or physical illness (1). Together, stress-related disorders in the broadest sense annually cause a hundred million years lived with disability (YLD). In 2013, major depression was the second leading cause of disability world-wide, while anxiety disorders ranked 9$^{th}$ (1). Not only do these numbers imply much individual suffering; they also indicate tremendous negative consequences for society. In Europe, for instance, the direct and indirect economic costs incurred by stress-related conditions have been estimated to be over €200 billion per year (2).

The high incidence of stress-related disorders is not new, and a worrying aspect of the epidemiological findings is that there has, on average, been no relevant decrease in numbers over the past decades (1). This is despite huge efforts spent on investigating the pathophysiology of these disorders and despite remarkable successes that have been made in understanding disease mechanisms and in developing effective treatments. A recent survey that attempted to identify reasons for the failure to reduce disease prevalence found that the lack of improvement can neither be attributed to an increase in risk factors, i.e., stressors, nor to greater public awareness of mental disorders or greater willingness to disclose (3). More likely reasons are that the provided treatments frequently do not meet minimal quality criteria ("quality gap") and that there are virtually no attempts to prevent disorders ("prevention gap"). In the four English-speaking countries included in the study, resources allocated to prevention and prevention research were found to be very small, and prevention efforts were somewhat provocatively characterized by the authors as "piecemeal" (3).

## Resilience research as an alternative strategy to promote mental health

We here argue that resilience research is a promising strategy to help close the prevention gap and thereby to complement traditional disorder-focused research. The science of resilience is based on the well-documented observation that many people maintain mental health despite exposure to severe psychological or physical adversity - a pattern that has been observed across different populations and types of adversities (4–6). Resilience research aims to understand why some people do not, or only temporarily, develop stress-related mental dysfunction, in spite of being subject to the same kind of challenges that cause long-term dysfunction in other people. This approach is naturally linked to the question of how to prevent stress-related disorders, rather than attempting to treat them at a later stage when significant individual suffering and societal and economic costs have already occurred (7). Resilience research, thus, is effectively a paradigm shift away from disease-focused towards health-focused research and from investigating pathophysiology towards investigating the mechanisms that can protect individuals against stress-related disease.

We therefore posit that resilience research is an important, or even necessary, complement to traditional pathophysiological research and has great potential for improving public health. We have reason to believe that this view is shared by many

in the mental health community: a Pubmed search with key words “resilience” and (“stress” or “trauma”) yields 76 entries for the year 2005 and 675 entries for 2015. In the same time period, the number of publications on “stress” or “trauma” did not even double (68% increase).

In this critical time when resilience research is surging and is about to establish itself as a new paradigm, some essential questions arise: How can we *now* shape and inform resilience research to make sure it will tangibly improve mental health science and practice? What can we do, at this stage, to put resilience research on the right track and to optimize the potential of this new line of research and also to avoid some of the pitfalls that have hampered the progress of disease-oriented research?

## Challenges to contemporary resilience research

A careful analysis of the results obtained to date and the methods currently used in resilience research (e.g., 8; 9) leads us to three key issues with significant bearing on future research. First, there is enormous heterogeneity in the way resilience is defined, operationalized, and measured and in the way resilience studies are designed. Therefore, when different researchers talk about resilience, they often use quite diverse concepts and their results are difficult to compare (9; 10). For example, the American Psychological Association on its website defines resilience as “the process of adapting well in the face of adversity, trauma, tragedy, threats or significant sources of stress” (www.apa.org/helpcenter/road-resilience.aspx). By contrast, some researchers consider resilience to be an ability or capacity, such as the ”ability to bounce back from negative emotional experiences” (11) or the “capacity to maintain competent functioning in the face of major life stressors“ (12). There is also the idea that resilience is a collection of various abilities and capacities (e.g., “the skills, abilities, knowledge, and insight that accumulate over time as people struggle to surmount adversity and meet challenges”; 13). While the latter definition suggests that the individual properties that define resilience may vary over time, a very popular trait-oriented perspective assumes that resilience is a fixed individual characteristic or predisposition (summarized in 14). As such, resilience is often juxtaposed to ”vulnerability” or “risk” in articles [320 hits in a Pubmed search with key words (“resilience [title]” and “vulnerability [title]”) or (“resilience [title]” and “risk [title]”) in February 2017]. One recent review concluded that “except for the main idea of facing challenges, it is somewhat difficult to guess that all of those definitions concern the same subject.” (15).

Second, it has been pointed out that predictors of resilient outcomes that have been identified so far are mostly weak, usually explaining only a small proportion of the variance in long-term mental health in stressor- or trauma-exposed study populations (4; 8; 9). In this vein, it is also still unclear whether combining multiple independent predictors will improve prediction, and the replicability of predictors across various populations still has to be evaluated much more extensively (4; 8; 9). Together, this means that it is currently impossible to say with any certainty whether an individual or a group of similar individuals will show no or only temporary impairments in mental health during and after stressor exposure. We will come back to this issue later.

And third, there is still a major gap between current resilience theory and the way empirical resilience research is often conducted. This last issue is of fundamental importance, and addressing it properly holds the key for finding a solution for the other issues.

## An operational definition of resilience

Since the seminal debate between proponents and critics of the resilience concept in the 1990's (summarized in 16), it is widely accepted among theorists that the maintenance or quick recovery of mental health during and after exposure to significant stressors (or also other positive outcomes such as academic success or social competence, which are of particular importance for resilience research in children and adolescents) results from a *dynamic process of adaptation* to the given stressful life circumstances (*Proposal 1*) (see also Table 1). Evidence for the process nature of resilience stems from a multitude of observations showing that individuals *change* while they successfully cope with stressors, whether this manifests at the level of altered perspectives on life (17–19), as emergence of new strengths or competences (16), as partial immunization against the effects of future stressors (20; 21), or even as epigenetic alterations and modified gene expression patterns (22; 23). In a remarkable homology, recent studies in animal models have been able to describe adaptive changes in the neural systems affected by stressor exposure specifically in animals that recovered well from stressor-induced behavioral dysfunctions; these studies also demonstrated the causal nature of these neural adaptations in recovery (24–27). To summarize, most resilience theorists currently agree that resilience is not simply inertia, or insensitivity to stressors, or merely a passive response to adversity, but the result of active, dynamic adaptation (28).

The process nature of resilience implies that resilience is *not a trait or stable personality profile*, or a specific genotype or some hard-wired feature of brain architecture (*Proposal 2*). Such predispositions may well contribute to positive adaptation, just as some other predispositions may make a person vulnerable to the effects of stressors. But taking seriously the insights gained by resilience theorists in the last decades means that it does not make much sense to equate resilience with a score on a resilience questionnaire or some value derived from a gene or blood test or a brain scan or any other one-time (cross-sectional) measure that is applied before adversity has occurred. In other words, resilience is not simply the flip-side of vulnerability. If, by contrast, resilience is increasingly being understood as the outcome of a dynamic process of successful adaptation to adversity, then, logically, *resilience should operationally be defined "ex post facto", that is as a good mental health outcome following an adverse life event or a period of difficult life circumstances* (29) (*Proposal 3*). In this logic, resilience cannot be measured in the absence of adversity, but only in response to stressful circumstances or potentially traumatizing events. Stable, trait-like characteristics or predispositions - which we term "resilience factors" - may make resilient responding to a stressor more likely, just as predispositions to vulnerability make resilient responding less likely; but they do so by facilitating the activation of intra-individual coping mechanisms or promoting beneficial interactions with the environment. Hence, resilience processes are distinct from resilience factors in that they always go along with neural, and often also behavioral activity, such as when someone uses his/her good cognitive emotion regulation capacity (a likely resilience factor) to actually exert emotion regulation in a stressful situation; or when someone's stress hormone release is limited through the action of some molecular negative feedback mechanism (the existence of a functional feedback system being another example of a hypothetical resilience factor); or when someone solves a social conflict or successfully seeks help by exploiting his/her good communication abilities (communication ability being yet another potential resilience factor). Another type of active resilience process is when experiences of adversity lead to an improvement or optimization of skills, capacities,

or behaviors, e.g., when someone is forced by new challenges to develop new emotion regulation strategies, making it likelier he/she will show optimized stress responses the next time he/she is challenged (9). Importantly, these dynamic processes or mechanisms themselves not only depend on a person's personality, or genotype, or brain architecture, but very much also on the nature of the stressor(s) and the complex and time-varying constellations of intra-, inter- and extra-individual circumstances present during and after stressor exposure. Hence, to be able to discover and understand resilience *mechanisms* (in the sense of the critical processes of successful adaptation), empirical resilience research must move from a static to a dynamic and process-oriented conceptualization. This has important consequences for study design.

## Consequences for study design

Contemporary resilience studies still often consider resilience as a score on one of the many available resilience questionnaires and correlate such scores with some other variable (e.g., personality, genotype, brain structure) in a cross-sectional design. The conclusion drawn from these studies is often that one has discovered the "resilient personality" or a "resilience gene" etc. This strategy implies either that resilience is a stable characteristic or predisposition (counter to our Proposal 2) or, alternatively, that resilient outcomes following adversity can be predicted by these questionnaires and, thus, the questionnaires can be used as surrogate markers for resilient outcomes that would otherwise have to be determined in tedious prospective studies. The latter assumption is also problematic because, if resilience results from a dynamic process of adaptation (see our Proposal 1), then it is relatively unlikely that a single baseline measure can satisfactorily predict a resilient outcome. Indeed, none of the current resilience questionnaires has been empirically validated as a good predictor of positive mental health outcomes following adversity in prospective studies (30). Other potential predictors such as specific personality properties usually only explain a few percent in outcome variance (8) and are not strong enough for individual prediction.

For these reasons, we would like to emphasize that, currently, there are no one-time (cross-sectional) resilience measures or surrogate or biomarkers of resilience and that, *at the present state, there is a pressing need for more prospective longitudinal studies on resilience* (*Proposal 4*). A prospective resilience study should consist of, ideally, a baseline assessment of the relevant outcome dimension (e.g., some mental health measure, or also any other index of psychosocial functioning relevant to the study population) before stressor exposure (T1) and, necessarily, an endpoint assessment of the outcome dimension, which should happen at a reasonable temporal distance from the offset of stressor exposure (T2) (9). In this simplest possible scenario, resilience can be operationalized as stable or only moderately deteriorated mental health (more generally, psychological function) despite stressor exposure. Stressor exposure itself has to be measured and quantified with as much detail as possible, because – evidently – moderate functional deterioration in somebody with massive stressor exposure is a more resilient outcome than moderate functional deterioration in somebody with only moderate stressor exposure. Hence, changes in mental health from T1 to T2 must be considered in relation to the adversity an individual has encountered (10). Such kinds of prospective studies may eventually identify valid outcome predictors - perhaps from patterns across multimodal data - that can then be used as surrogate markers in cross-sectional studies. However, measures of resilience based on longitudinal assessment are currently indispensable.

Beyond these minimum requirements for longitudinal resilience studies, a gold standard in study design that would permit researchers to even better align empirical resilience research with resilience theory involves measuring mental health/function at several time points during and after stressor exposure. Multiple sampling points allow for the delineation of trajectories of healthy responding that have already been shown in many different populations to range from stable mental health profiles with only small temporary disturbances ("minimal-impact resilience") to profiles of initial dysfunction followed by rapid recovery ("emergent resilience") (4; 8). Such careful phenotyping with high temporal resolution is a necessary basis for describing the presumably time-varying, individually variable and interactive engagement of the social, psychological and biological resilience processes (mechanisms) that generate the phenotypes. The monitoring of these mechanisms, then, should ideally also proceed with repeated measurements at high temporal resolution, as should the monitoring of stressor exposure. (Note that trajectory studies have so far mostly been conducted at time scales ranging from many months to a few years but will use much higher sampling frequencies in the future, owing to the possibilities of modern information technologies. However, even with much higher sampling rates, changes in mental health/function scores will still have to be present for at least a few weeks to be considered meaningful, i.e., not simply reflecting situational variation or noise. Meaningful changes in resilience mechanisms and stressor exposure, on the other hand, may as well occur on a much shorter time scale.)

Prospective studies conducted along these lines will in most cases come to include subjects that will experience different stressors at different times over the course of participation and will react with very different changes in mental health. Most study populations will thus contain more or less stressor-naïve as well as stressor-exposed subjects, allowing for comparisons akin to the comparisons between trauma-exposed and non-trauma-exposed subjects in traditional retrospective studies (e.g., in the field of PTSD research). In the same vein, these studies will permit comparisons between subjects with resilient and non-resilient (pathological) outcomes (e.g., absence or presence of a PTSD or depression diagnosis). Beyond these traditional – often binary - categorizations, the more fine-grained resolution of stressor exposure and mental health monitoring will, however, also permit statistical assessments based on continuous variables as well as the application of advanced modeling methods exploiting individual temporal dynamics to understand the dynamic and causal interactions between the included variables. Such process analyses will elucidate both pathological but notably also beneficial (resilient) adaptations.

## A review of prospective resilience studies with a focus on outcome prediction

To critically evaluate our claim that the current state of research does not permit conceptualization of resilience as a trait or predisposition, we reviewed the available prospective studies that attempted to identify baseline (T1) predictors of resilient outcome after stressor exposure (T2 or later). If studies that operationalize resilience in the way we here endorse show evidence for baseline factors that strongly and robustly predict mental health after adversity, this would substantially weaken our claim. To the contrary, it would suggest that resilience can to some extent be measured in the absence of adversity (e.g., by simply using a questionnaire or some behavioral or biological test at a single time point). Such surrogate measures or biomarkers could then replace the quantification of resilience in tedious and expensive prospective-longitudinal studies.

Consequently, we included only studies in our review in which subjects' mental health or psychological functioning was assessed at least once before a period of stressor exposure (baseline) and at least once after such a period (follow-up), in a

quantitative way. Because we were interested in identifying potential predictors of maintained or quickly recovering mental health despite adversity, we were not interested in studies where the baseline assessment involved only well-established predictors of mental health problems, such as pre-existing mental health problems or a life history of previous stressor exposure. Next, we did not consider studies where the amount or degree of stressor exposure between baseline and follow-up(s) was not well quantified. As argued above, stressor quantification is necessary to be able to test whether observed individual differences in stressor-induced mental health changes may simply be a consequence of individual differences in stressor exposure, which would be trivial. Hence, studies that simply reported a disease diagnosis (e.g., myocardial infarction or cancer) without a further qualification of the severity or duration of the disease were excluded, as were studies where a difficult life phase (e.g., war zone deployment, stressful professional training) was not further characterized in terms of the severity or number of specific events or challenges with which it was associated. In addition, where stressor exposure was quantified, it had to show a positive relationship to the development of mental health problems. Studies where this was not the case were excluded, as it was not clear in those studies whether the stressor(s) to which subjects were exposed were responsible for the reported mental health impairments. We also restricted our review to studies in adolescents and adults, to avoid the complications related to the very dynamic trajectories of change in children, which make outcome predictions particularly difficult. Finally, studies had to have group sizes of at least 30 subjects.

Among the remaining studies, one additional key criterion emerged. This can best be illustrated by two studies finding in different cohorts of soldiers that were assessed for post-traumatic symptoms both before and after war zone deployment that pre-deployment (baseline) military unit cohesion – an indicator of social support by comrades - negatively predicted post-deployment (follow-up) post-traumatic symptoms (31; 32). This suggests that unit cohesion, or more generally, social support, is a predictor of good mental health, which is a relevant and interesting finding. However, when taking into consideration a quantitative measure of deployment-related stressor exposure (combat exposure scale) by asking whether the interaction between unit cohesion and stressor exposure predicted post-deployment post-traumatic symptoms, there was no significant effect in either study (31: personal communication). In other words, pre-deployment unit cohesion in these studies did not moderate the effects of stressor exposure on post-traumatic symptoms. This, however, is the critical test when trying to answer the question whether a given baseline factor protects individuals against mental health deterioration in the face of adversity. Therefore, for the purpose of our review, it was not sufficient if a study merely corrected for effects of stressor exposure by using it as a covariate, and we only included studies that calculated predictor by stressor exposure interactions. From those studies, we only report the resulting moderation effects. Thereby, we ensured to only discuss *resilience* predictors, as opposed to global mental health predictors. An alternative strategy to take into consideration stressor exposure that was employed by some studies was to match a sample with stressor-related mental health impairments to a control sample with comparable stressor exposure but without corresponding mental health problems.

Table 2 shows all thirteen selected studies. Four reported null effects. Three studies expressed predictor effect sizes in terms of the proportion of variance in the follow-up outcome measure explained by the predictor. Percentages ranged between 5 and 13 (for trait self-enhancement, hair cortisol concentration, cortisol stress reactivity, and expression of specific gene networks). The maximum group size in these three

studies was 94, suggesting the results should be regarded as preliminary. Two studies expressed effect sizes in terms of odds ratios (ORs), which were in the small to very small range (0.82 – 7.5, for number of glucocorticoids in blood cells, perceived general health, and male gender). The lower ORs (0.82 and 1.46) were reported in a study with 2172 participants, whereas the comparatively high OR of 7.5 was reported in a study with only 68 participants, suggesting it should also be classified as preliminary. Four other studies did not quantify effect sizes. One identified resilience predictor, male gender (OR=1.46), was not significant in the four other studies in which it was tested. None of the other identified predictors has so far been tested for replication.

Overall, this literature review shows that the pattern of the potential resilience predictors identified so far is still very diverse and that there is no indication that any of the investigated predictors could be reasonably used as a surrogate marker for resilience, let alone be equated with resilience. That is, there is currently no empirical support for the popular idea that resilience is a predisposition. If anything, the existing data suggest that there may be multiple separate predisposing factors ("resilience factors" in our terminology), each of which has a small effect on outcomes. We conclude that it is clearly necessary to conduct more prospective resilience studies, a) to be able to better evaluate the predictive value of multiple baseline resilience factors, and b) to be able to address processes of adaptation occurring during and after stressor exposure, which is the focus of our recommendations. Note that this conclusion must be seen in the light of the limitations associated with our non-systematic review method, involving a lack of comprehensive searching and no formal quality assessment over and above the criteria explained above.

A final remark worth making is that any of the potential resilience factors listed in Table 2 could as well be framed as risk factors, by simply inverting their direction. For example, while high trait self-enhancement might be considered a resilience factor, one could as well call low self-enhancement a risk factor. This shows that research that only focuses on outcome predictors has little to add to traditional vulnerability research. Resilience research can make an original contribution to mental health science only where it investigates the dynamics of stressor adjustment.

## An invitation

Trying to align empirical research with theory in the field of resilience based on our Proposals 1 (process nature of resilience) and 2 (resilience is not a trait) has important practical consequences for how resilience is to be measured (Proposal 3: ex post facto) and for how studies are to be designed (Proposal 4: prospective). Notably, our operational definition of resilience as stable or only temporarily disturbed mental health despite adversity is not based on a single specific theory about what the crucial resilience mechanisms are and therefore does not presuppose the processes or mechanisms that produce the resilient outcome. It is much more open to scientific discovery than the mechanistic definitions most resilience questionnaires are based on (30), and it allows researchers from different theoretical schools to find a common basis and to compare their results. This will ultimately reduce much of the heterogeneity and confusion in the field and also reduce misperceptions in the interpretation of results by the public. It may well be that – as resilience research advances – our operational definition can be replaced by a definition of resilience that explicitly names specific predispositions, mechanisms

and interactive processes. We therefore only consider our approach a temporary, pragmatic solution that provides a suitable tool to advance research in the field.

By proposing that resilience be defined and studied based on outcomes in prospective studies, we do not want to argue against the search for resilience predictors or surrogate markers. As long as these are not confounded with resilience itself, improved predictors will help in the discovery of psychological or biological resilience mechanisms and can one day be useful in clinical decision-making. However, we strongly warn against terminology such as "resilience genes" or epigenetic "resilience mark(er)s" or neural "resilience networks" that promise more than they can deliver. In the era of large-scale genomics and hypothesis-free big biodata collection, we believe there is a big danger in an oversimplified use of the term resilience that will ultimately damage the field and prevent it from making the contribution to the science of mental health that we believe it can make.

We admit that the proposed approach, while surely more viable and promising than cross-sectional approaches, implies that we need to conduct resilience studies that are inevitably much more expensive, time-consuming and laborious. We are also aware that resilience research faces the special challenge that exposure to significant life stressors is rarely predictable and may be limited, even in high-risk cohorts such as deployed soldiers or other service members, and that base rates of maladaptive (non-resilient) outcomes can also be surprisingly low (4–6). If the majority of subjects in a study are either not heavily exposed or do not develop mental health problems, this obviously makes statistical analysis difficult. This problem is even bigger when the goal is to study cohorts that are representative for the general population, making large-scale multi-center studies indispensable. Hence, 21$^{st}$ century resilience research will be resource-demanding and challenging and can only be accomplished in an international collaborative effort, to which we herewith invite our colleagues. We are convinced that these efforts will eventually pay off by reducing mental suffering and the many other burdens associated with stress-related disease.

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642 TABLES
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| | |
|---|---|
| Proposal 1 | The maintenance or quick recovery of mental health during and after exposure to significant stressors results from a dynamic process of adaptation to the given stressful life circumstances. |
| Proposal 2 | Resilience is not a trait or stable personality profile, or a specific genotype or some hard-wired feature of brain architecture. Resilience should not be understood as a predisposition and, thus, is not the flip-side of vulnerability. We refer to stable resilience-conducive traits or other predispositions as “resilience factors“. |
| Proposal 3 | Resilience should operationally be defined “ex post facto”, that is as a good mental health outcome following an adverse life event or a period of difficult life circumstances. |
| Proposal 4 | At present, there is a pressing need for prospective longitudinal resilience studies. |

645 **Table 1. Proposals for future resilience research.**
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| **First author, year** | **Study population** | **Type of stressor** | **Main outcome** (d=dichotomous, c=continuous) | **Significant baseline outcome predictors** (positive results) | **Non-significant baseline outcome predictors** (negative results)* |
|---|---|---|---|---|---|
| Breen, 2015 (23) | Male marines (N=47 vs. 47; and 24 vs. 24) | War zone deployment | PTSD onset (d); post-traumatic stress symptoms (c) | Expression of gene network related to innate immune responses[§] (EV=10-13%) | |
| Clark, 2013 (33) | Male soldiers (N=253) | War zone deployment, previous trauma | Post-traumatic stress symptoms (c) | *COMT* genotype | |
| Eraly, 2014 (34) | Male marines (N=1719) | War zone deployment | Post-traumatic stress symptoms (c) | - | C-reactive protein (CRP) plasma levels |
| Gupta, 2010 (35) | College students (N=69) | Potentially traumatic events | Distress (c) | Trait self-enhancement (EV=8%) | Gender, social desirability, trait general optimism, trait neuroticism |
| Jenness, 2016 (36) | Adolescents (N=78) | Intense terror attack media coverage | Post-traumatic stress symptoms (c) | Trait reappraisal, trait catastrophizing[§] | Age, gender, trait rumination, trait problem solving |
| Kline, 2013 (31) | Soldiers (N=918) | War zone deployment | Post-traumatic stress symptoms (c) | - | Gender, unit cohesion[&], preparedness[&] |
| McAndrew, 2016 (32) | Soldiers (N=286; N=335) | War zone deployment | General mental health problems (c) | - | Unit cohesion, non-avoidant coping |
| Morin, 2017 (37) | Old-aged adults (N=1395) | Health events (cancer, stroke, heart disease, lung disease) | Depressive symptoms (c) | - | Age, gender, financial assets, education |
| Smid, 2015 (38) | Male soldiers (N=433) | Post-war zone deployment stressful life events | Post-traumatic stress symptoms (c) | T cell cytokine production[§] , innate cytokine production[§] | T cell-induced chemokines/IL-6 |
| Steudte-Schmiedgen, 2015 (39) | Male soldiers (N=90; N=80) | War zone deployment | Post-traumatic stress symptoms (c) | Hair cortisol concentration (EV=10%), cortisol stress reactivity (EV=5%) | Pre-deployment traumatic events, childhood trauma |
| Van Zuiden, 2011 (40) | Male soldiers (N=34 vs. 34) | War zone deployment | PTSD onset (d) | Number of glucocorticoid receptors (GRs) in blood cells[§] (OR=7.5) | mRNA expression of GR genes, *GILZ*, *SGK-1*, *FKBP5*; plasma cortisol |
| Wald, 2013 (41) | Male soldiers (N=1085) | War zone deployment | Post-traumatic stress symptoms (c) | Attentional threat bias[$], 5-HTTLPR genotype[$], their interaction | |
| Zhu, 2014 (42) | Older adults (N=2172) | Onset of moderate to severe pain | Depressive symptoms (c) | Perceived health (OR=0.82), male gender (OR=1.46) | Age, chronic illness |

648 *predictors that were tested but were not significant
649 [§]risk factor, i.e., predicting symptom worsening
650 [&]personal communication
651 [$]direction of effect depending on bias X genotype interaction term
652 PTSD, post-traumatic stress disorder; EV, explained variance; OR, odds ratio

653 **Table 2. Studies investigating baseline predictors of resilient outcome after stressor**
654 **exposure.**