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• Review

The questionnaire on autonomic regulation: a useful concept for integrative medicine?

Matthias Kröz[1,2,3,4], Marcus Reif[5], Danilo Pranga[1], Roland Zerm[1,2], Friedemann Schad[1,2], Erik Wim Baars[6], Matthias Girke[1,2]

1. Research Institute Havelhöhe, D-14089 Berlin, Germany
2. Department of Internal Medicine, Havelhöhe Hospital, D-14089 Berlin, Germany
3. Institute for Social Medicine, Epidemiology and Health Economics, D-10117 Berlin, Germany
4. Institute for Integrative Medicine, University of Witten/Herdecke, D-58313 Witten/Herdecke, Germany
5. Society for Clinical Research, D-10623 Berlin, Germany
6. Professorship Anthroposophic Healthcare, University of Applied Sciences Leiden, NL-2300 AJ Leiden, the Netherlands

ABSTRACT

The concept of autonomic regulation (aR) reflects the relevance of the function of different autonomic systems for health. aR can be captured by questionnaires. We differentiate between a trait or constitutional aR questionnaire version including 12 (short-version) or 18 items, respectively, with three subscales (orthostatic-circulatory, rest/activity and digestive regulation), and an 18-item state aR questionnaire on the preceding week with four subscales (rest/activity, orthostatic-circulatory, thermo- and digestive regulation). The validated questionnaires show satisfying to good reliability and robust validity with clear construct validity. In this article, we summarized the actually available literature on aR and the use of aR questionnaires in clinical and observational studies. We described the relationship of high aR with health and in case of low aR or loss of regulation with disease and functional disorder in the three (four) different subscales and functional systems, such as rest/activity, orthostatic-circulatory or digestive regulation (thermoregulation) with the consecutive therapeutic need. Finally, we gave perspectives of its further application in clinical research.

Keywords: anthroposophic medicine; autonomic regulation; delivery of health care; integrative medicine; questionnaire

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1 Introduction

Over the last two decades, patient-reported outcomes (PROs) such as health-related quality of life (HRQL) have received major attention in medicine in general and particularly in patient-centred disciplines[1,2]. Integrative medicine in general and anthroposophic medicine in particular are characterized by an intensive patient-physician relationship with a large impact of patient preferences and PROs[3]. The National Center for Complementary and Integrative Health (NCCIH, the former NCCAM) defines integrative medicine as a combination of conventional medical treatment with complementary and alternative medicine with some high-

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Correspondence: Matthias Kröz, MD; E-mail: mkroez@havelhoehe.de

quality evidence of safety and effectiveness[4]. Other definitions comprise a broader conceptualization. For example, the Consortium of Academic Centers in the United States which extends the NCCIH's definition to include the patient's perspective, the patient-physician relationship, and the healing orientation[5]. In anthroposophic medicine other elements are taken into consideration, such as the integration of the individual and the biographical perspective[3,6].

A PRO-based approach for the evaluation of integrative medicine requires constitutional, salutogenesis-[7] and hygiogenesis-orientated[8] questionnaires along with conventional standard HRQL questionnaires. Gutenbrunner distinguishes between salutogenesis as more psychological, and hygiogenesis as more physiological-based self-healing process[9]. A meta-analysis showed established questionnaires on HRQL to be higher correlated with mental health than with physical health[10]. Therefore, we decided to focus on health in capturing autonomic (physiological) function and regulation. We define autonomic regulation (aR) as the state of regulation of different autonomic functions in the rhythmical change of rest and activity. aR is influenced by constitution, gender, age and disease. In healthy people, aR is a relatively stable trait. Acute illness and chronic conditions lead to reduced aR; this is known as loss of regulation[11,12]. A far-ranging number of autonomic parameters have been investigated in chronobiological research and have shown—for both rhythmically well synchronised and de-synchronised conditions—a strong impact on health or chronic conditions, HRQL and symptom burden[13]. In 1920, Rudolf Steiner had already proposed the idea of focusing on autonomic functioning in the context of anthroposophic medicine to obtain information about the mind-body-spirit balance. He postulated the idea that mind/spirit (ego-organization) would significantly regulate the autonomic functioning[14].

In this article we introduce the conceptual framework of the questionnaires on aR which have been developed in order to evaluate the constitutional background and to add a hygiogenetic-based practical outcome measure for general medicine and particularly for anthroposophic and integrative medicine.

2 The trait concept, the questionnaires on aR and their reliability and validity

Based on preparatory work from Weckenmann *et al*[15] the first approach was to develop a rather constitutional-orientated scale capturing autonomic functions on sleep latency, sleep quality, dream recall, ability of pulling oneself together, daytime wellbeing, orthostatic function, acral thermoregulation and sweating. Based on these items, a first short version questionnaire on aR was developed consisting of 12 items with sufficient internal consistency and good test-retest reliability and validity[16]. In a further step we evaluated items on digestion, constipation, bowel movement and frequency and integrated them into the aR concept in the context of a large validation study. This led to an 18-item questionnaire on aR with three subscales including orthostatic-circulatory, rest/activity, and digestive regulation, which showed satisfying internal consistency, good test-retest reliability, and convincing factor about analytical differentiation between the subdomains[12]. The validity analysis revealed positive correlations between high aR and health, better HRQL, better personality presence and thermoregulation[16]. These results are compatible, on a correlative level, with Steiner's conception of a mind-body-spirit balance without proving it and support the aR theory that a highly regulated and high-performing autonomic functioning is associated with psycho-physiological indicators of mental balance[14] (Table 1).

3 State aR

The trait version on aR showed a good reliability and validity as described above, but it remained unclear how to differentiate between constitution (how autonomic functions are in general) and the actual state of regulation. Therefore, we started a further validation study to generate a new scale on state aR reflecting the preceding week. All items were adapted from the trait version to questions showing a clear relation to the preceding week. Some items could not be adapted, such as "dizziness from circular motions (when on a roundabout)" and "travel sickness". Other items were more specific such as "sweating even after light physical activity", "fine motor skills", "cold hands or feet" (Table 1). Based on a factor analysis a four-subscale structure was generated (rest/activity, orthostatic-circulatory, thermoregulation and digestive regulation) with a good internal consistency, satisfying test-retest reliability and item total correlation. There was a good concurrent validity with the trait aR-scale and sufficient convergent validity (health, less depression, anxiety, fatigue, better Karnofsky-performance index, thermoregulation, personality marker and HRQL) including a robust discriminant validity and responsiveness (Table 1)[17].

4 Languages in which questionnaire translations and validations are available

Along with the German original version, forward-backward translations based on the International Society for Pharmacoeconomics and Outcomes Research (ISPOR)

criteria are now available in English and Dutch[18]. Translations into French (Ballivet & Gelin), Italian (Portalupi), and Spanish (Villegas & Kergel) have been carried out on the basis of a forward translation. Along with the German questionnaires on trait and state aR[19], the Dutch State aR version, which has a factor structure, reliability, and validity comparable to the German version, has also been validated[20]. A validation study on the trait and state version of the English version has also been carried out; however, the results of the validation have not been published yet[21].

5 What is the clinical use and relevance of aR?

A number of studies have shown a reduced aR in breast cancer patients and patients with diabetes mellitus type 2 compared to healthy controls (Table 2). In both patient groups, most examinations have shown that this is associated with a reduced rest/activity regulation, pointing towards cancer-related fatigue (CRF) syndrome, associated circadian and sleep problems in breast cancer patients and other cancer patients, and sleep disorders in diabetes mellitus type 2[12,22]. These changes in rhythms are still present in long-term breast cancer survivors after more than ten years[23]. The autonomic impairments captured here can be linked to the complex CRF problems consisting of chronic inflammation, sleeping disorders, neuro-immunological, and endocrine problems[24] summarised by Miller *et al*[25] in their description of the conceptual framework. They can be improved by means of a multimodal therapy concept consisting of psycho-education, sleep education, eurythmy, and art therapy with regards to CRF, sleep disorders, and aR[26]. However, a pilot study showed that aR had no predictive significance for improvement of CRF[27]. In patients suffering from diabetes mellitus type 2, a reduced aR is strongly associated with sleep apnea syndrome (SAS) and therefore points towards impaired sleep quality and increased daytime sleepiness[12]. In comparison, patients with colorectal cancer do not have a reduced aR[11]. Although an observational study showed that aR had no impact on survival in breast and colorectal cancer patients as well as healthy controls after 6.6 years[28], it did have an impact on long-term CRF, cognitive fatigue, anxiety, and depression in the context of a multivariate analysis[23].

Interestingly, a current study has shown that aR in

Table 1 Versions of trait and state autonomic regulation questionnaire

Regulation	Trait autonomic regulation (trait aR)	State autonomic regulation (state aR)
Orthostatic-circulatory regulation	TaR1: dizzy spells TaR5: dizziness when looking down TaR6: dizziness when getting up in the morning TaR9: dizziness when straightening up or bending down TaR11: cold or cold-sweaty hands TaR15: travel sickness TaR16: dizziness from circular motions	SaR3: dizzy spells/ turning around SaR12: dizziness when getting up in the morning SaR14: dizziness when turning around quickly SaR17: dizziness when getting up or bending down
Rest/activity regulation	TaR2: pulling oneself together to go to work TaR3: rested in the morning TaR4: problems falling asleep TaR7: tend to sweat TaR8: suffering from disturbed sleep TaR10: time of the day feeling most comfortable TaR17: sweating at night TaR18: stomach rumbling	SaR1: cold hands or feet SaR5: fall asleep SaR8: pulling oneself together to do things SaR9: rested in the morning SaR10: stomach rumbling SaR11: felt less competent and skilful than usual SaR15: restless sleep SaR18: cold and sweaty hands or feet
Digestive regulation	TaR13: bowel movements frequency TaR14: bowel movements regularly TaR19: constipation	SaR2: bowel movements frequency SaR4: bowel movements regularly/ same time SaR6: constipation
Thermoregulation		SaR7: sweating at night SaR13: tend to sweat SaR16: sweating during light physical activity
Additional questions	TaR12: remember dreaming	SaR19: feel most comfortable

Overview of the short and long version questionnaire on trait autonomic regulation (trait aR) and the state version questionnaire (state aR) including the factors structures. Items from the trait autonomic regulation are abbreviated in the table TaR1, TaR2…, from the state autonomic regulation SaR1, SaR2… The sum scale of the trait aR is constituted by the items TaR1–TaR11 and TaR13–TaR19. In the trait aR questionnaire a short version scale is available, consisting of the items TaR1–TaR12. The state aR sum scale is constituted by SaR1–SaR18.

Table 2 Overview of the studies, showing a loss of trait autonomic regulation in different patient groups including their subscales

Conditions and number of available studies (*n*)	aR short (12 items) and long (18 items) version	aR subscales		
		Rest/activity regulation	Orthostatic-circulatory regulation	Digestive regulation
Oncological diseases				
Breast cancer (5)	-1–4, 8	-3, 4	-4	
Colorectal carcinoma (2)				
Cancer various (1)		-5		-5
Diabetes mellitus				
Type 2 (4)	-1**, 2, 3*, 6	-3*	-3*	
Type 1 (3)	-7			
CHD (2)	-2			
Sleep apnea (1)	-10			
Autoimmune diseases				
Rheumatic diseases (2)	-2, 3		-3	
Hashimoto's disease (2)				-3
Multimorbid (2)	-2, 3	-3	-3	-3
Healthy				
Elderly people (2)	-9			
Women (4)	-2, 3, 6*		-3	-3

The above table shows the patient and study groups examined. The figures in parentheses show the number of existing studies available. Significant differences (P<0.05) which show a lower aR of patient groups compared to healthy controls, and females compared to males respectively, are shown as "-". *: Test (P<0.05) has not been published so far. **: Differentiation between diabetes mellitus type 1 and type 2 see 7. Numbers 1–10 in the table refer to the number of references of this review corresponding to the available studies (1: [16]; 2: [11]; 3: [12]; 4: [22]; 5: [19]; 6: [32]; 7: [35]; 8: [23]; 9: [33]; 10: [29]) modified based on [36]. aR: autonomic regulation; CHD: coronary heart diseases.

patients with diabetes mellitus type 2 and concomitant SAS is significantly lower than in diabetes patients who do not suffer from SAS, and that these latter patients in turn show lower values compared to the healthy controls. This points towards the fact that patients with diabetes mellitus type 2 have further changes in aR beyond SAS which cannot be captured with common questionnaires such as the Epworth Sleepiness Scale[29]. On the other hand, patients with coronary heart disease showed no significant loss of regulation in studies carried out with the long version[12], whilst a study carried out with the short version showed a reduction of aR[11] (Table 2).

Patients with rheumatic disorders also showed reduced aR compared to healthy controls; however, this was associated with loss of regulation with regard to orthostatic-circulatory aR. Psychiatric patients with dissociative symptoms showed tight correlations with hysterical, functional impairments (F-P-Score) and inverse correlations with the sensitivity scale in the mental state scale (Befindlichkeits-Skala (Bf-S))[30]. This can be understood as confirmation of the conceptual hypothesis that low aR is associated with dissociative symptoms, loss of integrity and low development of personality presence in psychiatric patients[12]. In shift workers low-trait aR values have been captured[31].

Several studies have found lower aR in healthy females compared to healthy males[12,32]. This indicates differences on gender constitution and introspection. The overview graphic shows moderate correlations between aR, HRQL, internal coherence and low to moderate correlations with subjective health and self-regulation (Figure 1).

In a group of relatively healthy, older study participants aR showed weak to moderate correlations with geriatric basis-assessment instruments such as the cumulative illness rating scale (CIRS), physical self-maintenance scale (PSMS/ADL) or geriatric depression scale (GDS) in a comparable way to the geriatric assessment scales amongst one another. Therefore, the aR questionnaire appears as a suitable instrument for short pre-screening[33]. Furthermore, older people showed lower aR than young, healthy ones, which points towards age-related loss of aR[33]. These results require further verification also with

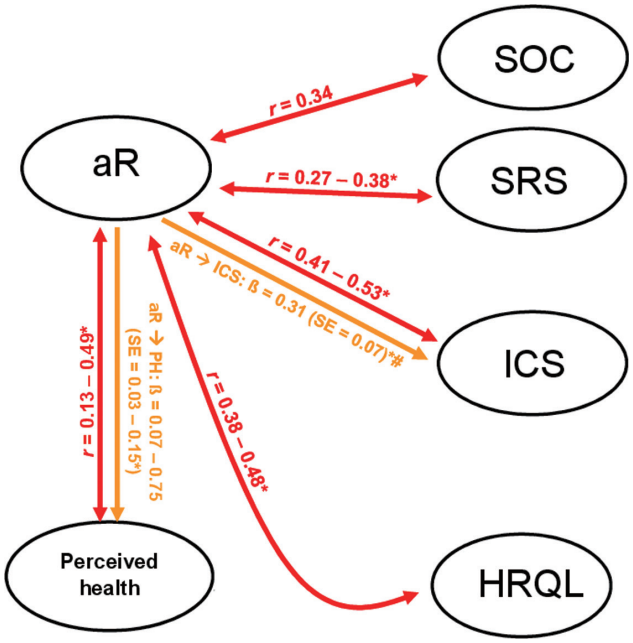

Figure 1 Interactions between trait autonomic regulation (aR) and self-regulation (SRS), internal coherence (ICS), sense of coherence (SOC), health-related quality of life (HRQL) and perceived health

Connections which originate from aR are shown in red (correlations) and orange (regressions). Correlations are shown as red arrows in both directions. Results from prospective regressions are shown as orange arrows in one direction. [12,16,23,37–40] (Klaus unpublished) modified based on [36]. *: P <0.05; #: unpublished.

regards to insufficient reliability in the very aged[33]. A respective study is currently carried out.

At the current status of evaluation a classification and a manual for both aR scales are not available and their respective English validation is not yet published. Therefore, the interpretation is limited in the individual case. Nevertheless, the practitioners can apply the aR scales, thereby expanding classical diagnostics to get an idea in which subscale and level patients have indicators for a rather low aR or loss of regulation (rest/activity, orthostatic-circulatory, digestive regulation, and in the state aR also thermoregulation). Based on these results a regulatory and constitutional pharmacological or non-pharmacological treatment can be defined. Such examples are mistletoe treatment and its possible influence on stabilization of rest/activity regulation in cancer patients[17]. Other possible indications can be discussed for eurythmy or music therapy in anthroposophic medicine or for specific acupuncture procedures in Chinese medicine.

6 Perspectives of application

In summary, the first studies on the clinical relevance of aR are encouraging and point towards differentiated results depending on diseases, has strong correlations with health and illness, even though the reliability in people aged over 85 requires further verification. Looking ahead, we will have to conduct conceptual and empirical research for a better understanding of physiological mechanisms and relationship of aR and health. In a new concept health was introduced as "the ability to adapt and to self-manage in the face of social, physical and emotional challenges"[34]. Such an adaptive definition of health has a clear association with the conceptual framework of aR and opens new applications of aR questionnaires in future research. Furthermore, we will have to clarify whether therapy concepts adapted to empirical aR measurements can contribute to an optimisation of therapy in general medicine and particularly in anthroposophic and integrative medicine. Further prospective, interventional and observational long-term studies are required to answer the question that to which extent aR is a reliable prognostic factor for CRF, diabetes mellitus type 2 or geriatric patients.

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8 Competing interests

The authors declare no competing interests.

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