

Efficacy of repeated immunoadsorption in post-COVID ME/CFS



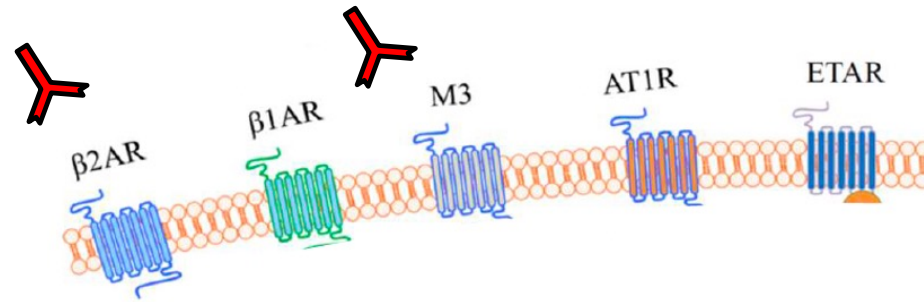
Institut für
Medizinische
Immunologie



Dr. Elisa Stein | 13.05.2025 |

International ME/CFS Conference 2025

GPCR Autoantibodies



- natural regulatory autoantibodies
- $\beta 2$ adrenergic receptor antibody function is impaired in ME/CFS
- Correlation of elevated $\beta 2$ adr rec antibody levels with symptom severity in ME/CFS
- Clinical trials targeting autoantibodies provide first evidence of efficacy in ME/CFS

1. Loebel M, et al. Antibodies to β adrenergic and m cholinergic receptors in patients with ME/CFS. *Brain Behav Immun.* 2016
2. Hartwig J, et al. IgG stimulated $\beta 2$ adrenergic receptor activation is attenuated in patients with ME/CFS. *Brain Behav Immun Health.* 2020
3. Freitag H, et al. Autoantibodies to Vasoregulative GPCR correlate with Symptom Severity, Autonomic Dysfunction and Disability in ME/CFS. *J Clin Med.* 2021
4. Scheibenbogen C, et al. Immunoadsorption to remove $\beta 2$ adrenergic receptor antibodies in ME/CFS. *PLoS One.* 2018

Observational studies on immunoadsorption in pre-pandemic ME/CFS



RESEARCH ARTICLE

Immunoadsorption to remove β_2 adrenergic receptor antibodies in Chronic Fatigue Syndrome CFS/ME

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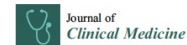
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Abstract

Introduction

Infection-triggered disease onset, chronic immune activation and autonomic dysregulation in Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME) point to an autoimmune disease directed against neurotransmitter receptors. We had observed elevated autoanti-



Article

Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Efficacy of Repeat Immunoadsorption

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Abstract: (1) Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is a complex neuroimmunological disease. There is evidence for an autoimmune mechanism for ME/CFS with an infection-triggered onset and dysfunction of β_2 -adrenoreceptor antibodies (β_2 AR-AB). In a first proof-of-concept study, we could show that IA was effective to reduce β_2 AR-AB and led to improvement of various symptoms. (2) Five of the ME/CFS patients who had clinical improvement following treatment with a five-day IA were retreated in the current study about two years later with a modified IA protocol. The severity of symptoms was assessed by disease specific scores during a follow-up period of 12 months. The antibodies were determined by ELISA. (3) The modified IA treatment protocol resulted in a remarkable similar clinical response. The treatment was well tolerated and 80–90% decline of total IgG and β_2 AR-AB was achieved. Four patients showed a rapid improvement in several clinical symptoms during IA therapy, lasting for six to 12 months. One patient had no improvement. (4) We could provide further evidence that IA has clinical efficacy in patients with ME/CFS. Data from our pilot trial warrant further controlled studies in ME/CFS.


Observational study on immunoadsorption in post Covid ME/CFS

Procedure: 5 sessions of immunoadsorption within 10 days in an outpatient setting, responders receive a 2nd cycle after deterioration

PATIENTS

20 patients with post-COVID ME/CFS and elevated β 2 AR-AB (>14 U/l)

Gender:  $n = 13$

 $n = 7$

Age : 40 years (IQR: 36–51)

Duration of illness: 22 month (IQR: 15–31)

Bell-Score: 30-40

Primary endpoint:

Improvement of at least 10 points in the SF-36 PF four weeks after immunoadsorption

Further surveys: COMPASS31, FSS, Bell Skala, DSQ-PEM, NRS

Hand grip strength → muscle fatigue

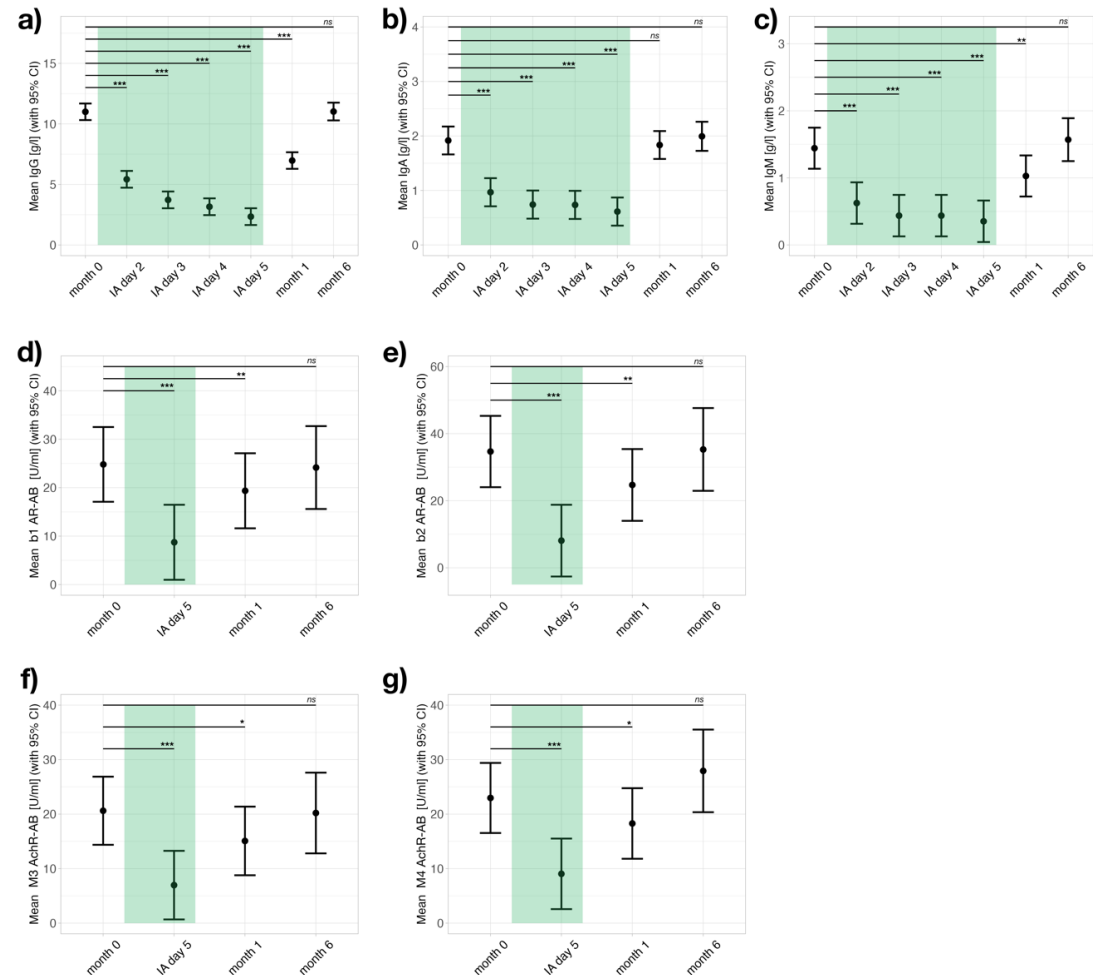
EndoPAT → endothelial dysfunction

Course of immunoglobulins and autoantibodies

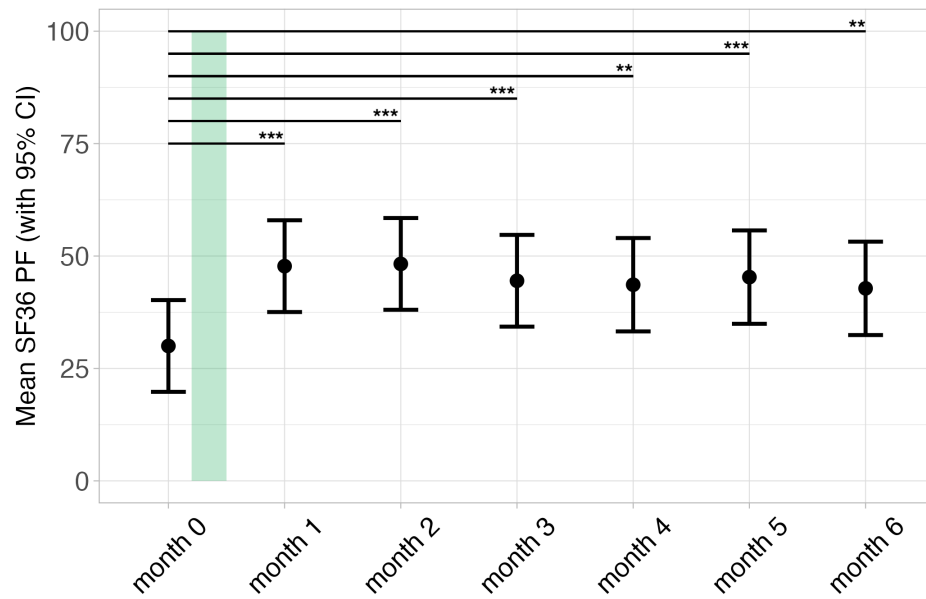
Significant reduction of all immunoglobulins on day 5 of immunoadsorption ($p < 0.001$)

- IgG: 79% (CI: 73 – 84%)
- IgA: 68% (CI: 63 – 78%)
- IgM: 76% (CI: 58 – 93%)

Significant reduction of Autoantibodies on day 5 of immunoadsorption ($p < 0.001$)

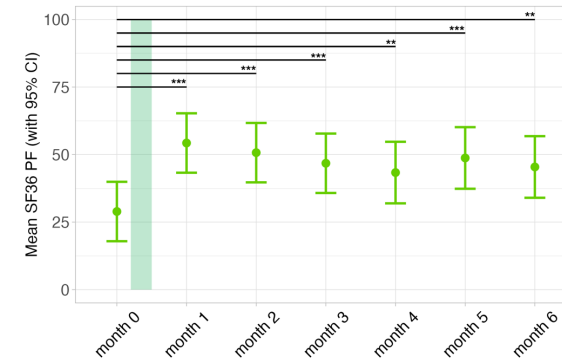


Course of symptoms - SF36 Physical Functioning



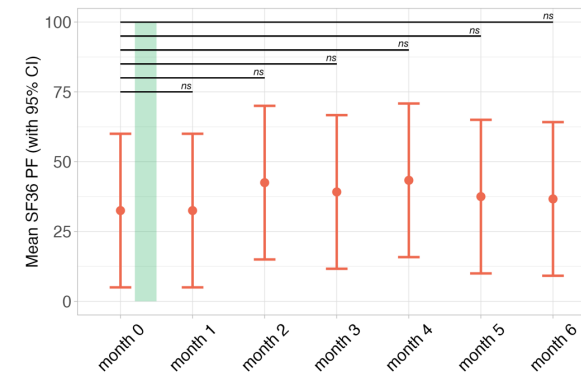
n = 20

responder



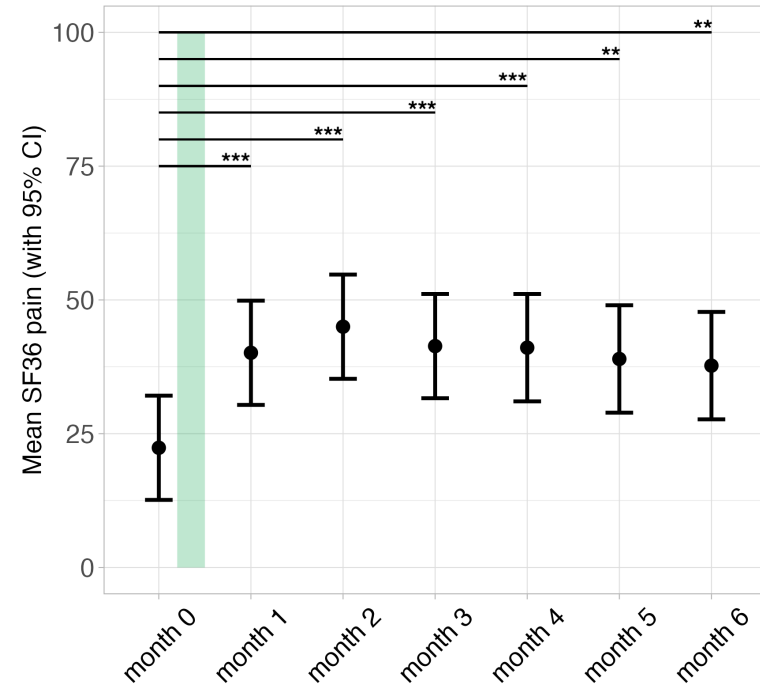
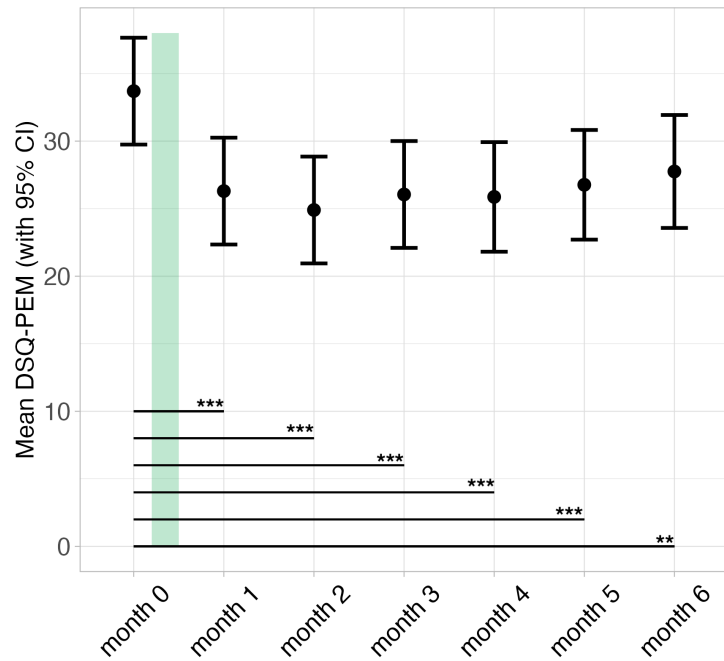
n = 14

Non- responder



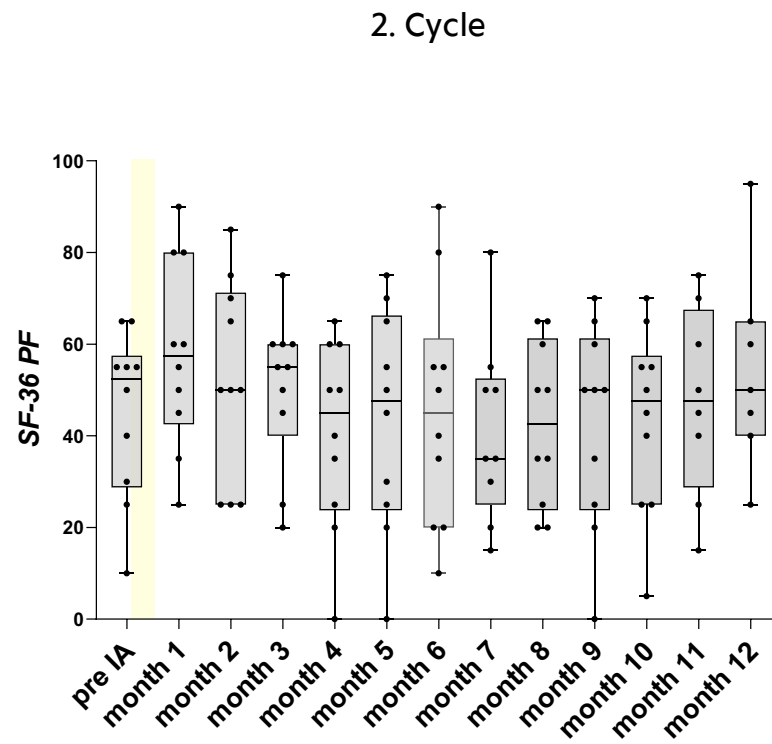
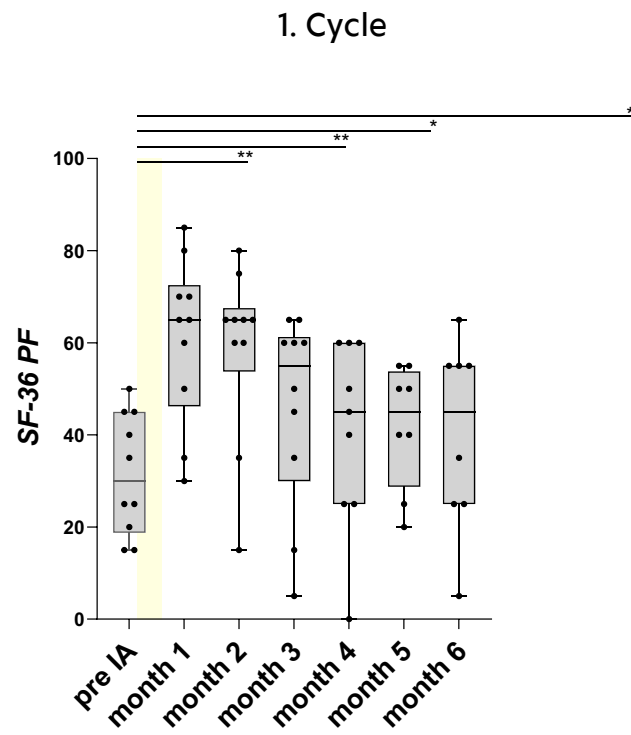
n = 7

Course of symptoms– selected further symptoms



n = 20

Course of symptoms in SF36 PF in patients receiving a second immunoadsorption



Observational study on immunoadsorption in Post Covid ME/CFS

Conclusion: immunoadsorption is effective in patients with post-COVID fulfilling ME/CFS criteria and elevated β 2-adrenergic-autoantibodies.

Role of immunoadsorption in future treatment of ME/CFS?

- RCT is currently taking place in Berlin
- Limited availability and limited efficacy
- **Combination with CD19 or CD20 monoclonal antibodies depleting autoantibody-producing B cells**

Causes for response vs. non-response?

- B-cell subtyping (CyTOF) (Birgit Sawitzky)
- Measurement of further AAB
- Markers for immune dysregulation

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Chronisches Erschöpfungssyndrom
(CFS/CHDS/ME)



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Charité Fatigue Centrum

Nationale Klinische Studiengruppe (NKSG) ME/CFS und Post-COVID-19-Syndrom

NKSG Nationale Klinische Studiengruppe ME/CFS PCS

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Die Nationale Klinische Studien Gruppe (NKSG) ist ein interdisziplinäres Netzwerk von Ärzten und Wissenschaftlern mit dem Ziel, translationale Forschung und Therapiestudien für die Behandlung von Myalgischer Enzephalomyelitis/Chronischem Fatigue-Syndrom (ME/CFS) und Post-COVID-19-Syndrom (PCS) zu entwickeln.

Etwa jede/r Zehnte leidet nach einer leichten bis mittelschweren COVID-19 unter anhaltenden Beschwerden, darunter häufig schwere Fatigue und Belastungsintoleranz. Halten diese Symptome mehr als vier Wochen an, spricht man von Long COVID. Als Zustand nach COVID-19 oder PCS hat die Weltgesundheitsorganisation (WHO) Symptome definiert, die das tägliche Leben beeinträchtigen, mehr als drei Monate nach der Infektion bestehen und mindestens zwei Monate andauern. Am häufigsten sind jüngere, bis dahin gesunde Frauen betroffen. Wie eine aktuelle Studie der Charité zeigt, entwickelt ein Teil der PCS-Patientinnen und Patienten ME/CFS – eine komplexe, chronische Erkrankung mit unterschiedlich ausgeprägten Symptomen, darunter schwere Fatigue und Belastungsintoleranz, Konzentrationsstörungen,

Further information: https://cfc.charite.de/klinische_studien/nksg/

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