

Beyond the Symptom: The Biology of Fatigue
September 27 – 28, 2021

Fatigue in neurological disorders: the sensory attenuation hypothesis

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# Disclaimer and Disclosures

### Disclaimer

This certifies that the views expressed in this presentation are those of the author and do not reflect the official policy of the NIH.

### **Disclosure**

This certifies that I, Anna Kuppuswamy, have no financial relationship that is relevant to the subject matter of this presentation.



# Apathy and fatigue

Temporal Associations between Fatigue,
Depression, and Apathy after Stroke:
Results of the Cognition and Affect after
Stroke, a Prospective Evaluation of Risks Study

Elles Douven<sup>a</sup> Sebastian Köhler<sup>a</sup> Syenna H.J. Schievink<sup>a</sup>
Robert J. van Oostenbrugge<sup>b</sup> Julie Staals<sup>b</sup> Frans R.J. Verhey<sup>a</sup> Pauline Aalten<sup>a</sup>

#### RESEARCH ARTICLE

Open Access

Apathy/depression, but not subjective fatigue, is related with cognitive dysfunction in patients with multiple sclerosis

Masaaki Niino<sup>1\*</sup>, Nobuhiro Mifune<sup>2</sup>, Tatsuo Kohriyama<sup>3</sup>, Masahiro Mori<sup>4</sup>, Takashi Ohashi<sup>5</sup>, Izumi Kawachi<sup>6</sup>, Yuko Shimizu<sup>7</sup>, Hikoaki Fukaura<sup>8,9</sup>, Ichiro Nakashima<sup>10</sup>, Susumu Kusunoki<sup>11</sup>, Katsuichi Miyamoto<sup>11</sup>, Kazuto Yoshida<sup>13</sup>, Takashi Kanda<sup>13</sup>, Kyoichi Nomura<sup>9</sup>, Takashi Yamamura<sup>14</sup>, Fumihito Yoshii<sup>15</sup>, Jun-ichi Kira<sup>16</sup>, Shunya Nakane<sup>17</sup>, Kazumasa Yokoyama<sup>18</sup>, Makoto Matsui<sup>19</sup>, Yusei Miyazaki<sup>20</sup> and Seiji Kikuchi<sup>20</sup>

## The associations between fatigue, apathy, and depression in Parkinson's disease

Skorvanek M, Gdovinova Z, Rosenberger J, Ghorbani Saeedian R, Nagyova I, Groothoff JW, van Dijk JP. The associations between fatigue, apathy, and depression in Parkinson's disease. Acta Neurol Scand 2015: 131: 80–87.

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M. Skorvanek<sup>1,2,3</sup>, Z. Gdovinova<sup>1,2</sup>, J. Rosenberger<sup>3</sup>, R. Ghorbani Saeedian<sup>3,4</sup>, I. Nagyova<sup>3,4</sup>, J. W. Groothoff<sup>5</sup>, J. P. van Dijk<sup>3,5</sup>

Apathy and fatigue co-occur but are dissociable

# Is effort-reward trade-off a result or driver of fatigue?

Effort but not Reward Sensitivity is Altered by Acute Sickness Induced by Experimental Endotoxemia in Humans

Amelia Draper<sup>1</sup>, Rebecca M Koch<sup>2</sup>, Jos WM van der Meer<sup>3</sup>, Matthew AJ Apps<sup>1</sup>, Peter Pickkers<sup>2,5</sup>, Masud Husain<sup>1,5</sup> and Marieke E van der Schaaf<sup>\*,4,5</sup>

Department of Experimental Psychology University of Oxford, Oxford, UK; <sup>2</sup>Department of Intensive Care Medicine, Radboud University Medical Center, Nijmegen, The Netherlands; <sup>3</sup>Department of Internal Medicine, Radboud University Medical Centre, Nijmegen, The Netherlands; <sup>4</sup>Donders Institute for Brain, Centre for Cognitive Neuroimaging, Cognition and Behaviour, Radboud University, Nijmegen, The Netherlands

# Dissociation between mental fatigue and motivational state during prolonged mental activity

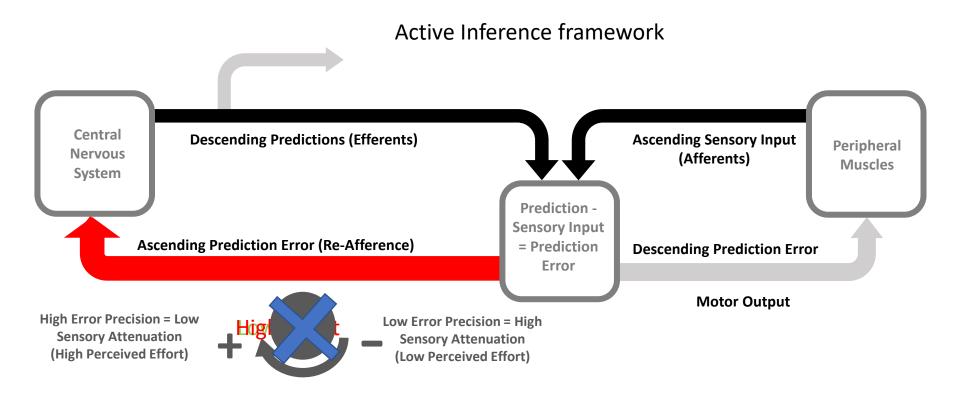
Mónika Gergelyfi, Benvenuto Jacob, Etienne Olivier and Alexandre Zénon\*

Institute of Neuroscience, Université Catholique de Louvain, Brussels, Belgium

Fatigue maybe unrelated to changes in reward sensitivity, but related to perceived effort

<sup>&</sup>lt;sup>a</sup>Department of Psychiatry and Neuropsychology, Maastricht University, School for Mental Health and Neuroscience (MHeNs), Alzheimer Center Limburg, Maastricht, The Netherlands; <sup>b</sup>Department of Neurology, Cardiovascular Research Institute Maastricht (CABIM), Maastricht University Medical Center (MUMCH), Maastricht The Netherlands

# Sensory attenuation (SA) model of fatigue – proprioception



Greater perceived effort maybe explained by abnormal weighting of sensory prediction error

## Behavioural evidence of SA in a motor task

ARTICLE

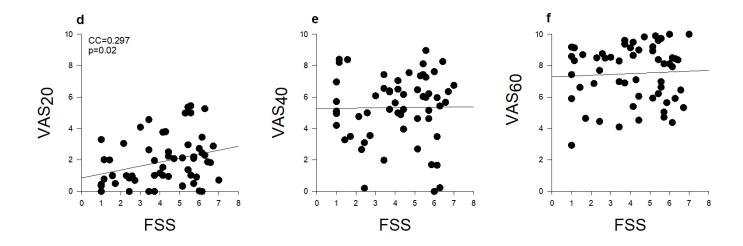
OPEN ACCESS

# Exploring the relationship between effort perception and poststroke fatigue

William De Doncker, MSc, Lucie Charles, PhD, Sasha Ondobaka, PhD, and Annapoorna Kuppuswamy, PhD Neurology® 2020;95:e3321-e3330. doi:10.1212/WNL.000000000010985

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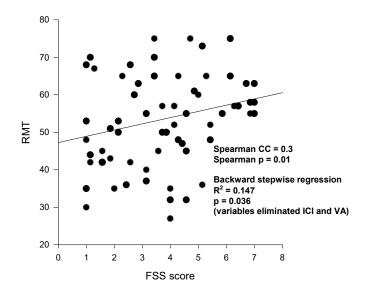


Altered perceived effort in fatigue can be explained by poor sensory attenuation

# Neurophysiological evidence

## Post-stroke fatigue: a deficit in corticomotor excitability?

Annapoorna Kuppuswamy, Ella V. Clark, Isobel F. Turner, John C. Rothwell and Nick S. Ward



Fatigue is associated with neurophysiological markers of poor behavioural flexibility



Contents lists available at ScienceDirect

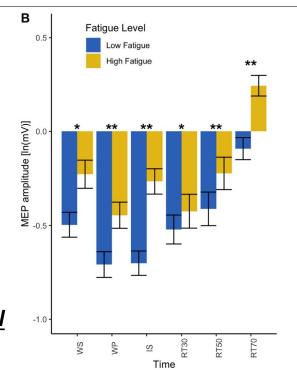
#### Clinical Neurophysiology

journal homepage: www.elsevier.com/locate/clinph

Influence of post-stroke fatigue on reaction times and corticospinal excitability during movement preparation

William De Doncker a,\*, Katlyn E. Brown a,b, Annapoorna Kuppuswamy a

b University of Waterloo, Department of Kinesiology, Faculty of Applied Health Sciences, Waterloo, ON, Canada

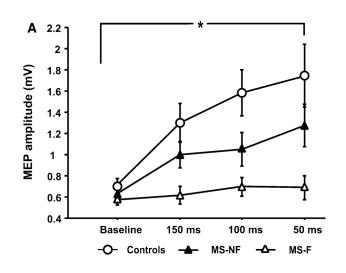


J Neurol (2011) 258:263–272 DOI 10.1007/s00415-010-5742-x

#### ORIGINAL COMMUNICATION

## Is central fatigue in multiple sclerosis a disorder of movement preparation?

Francesca Morgante · Vincenzo Dattola · Domenica Crupi · Margherita Russo · Vincenzo Rizzo · Maria Felice Ghilardi · Carmen Terranova · Paolo Girlanda · Angelo Quartarone



<sup>&</sup>lt;sup>a</sup> Department of Clinical and Movement Neuroscience, Institute of Neurology, University College London, UK

# Visual and auditory effort

Disease Mechanisms

# The Neurobiology of Pathological Fatigue: New Models, New Questions

Annapoorna Kuppuswamy<sup>I</sup>

ons

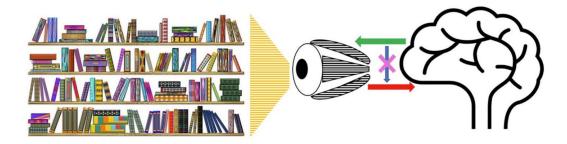
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The Neuroscientist

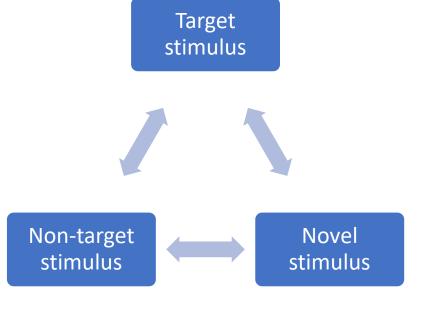
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## **Poor Saccadic Suppression**



<u>Can poor sensory attenuation also explain greater</u> visual effort?

## Perceptual load limitations



Can poor ability to switch attention explain visual and auditory effort?

# Target Vs distractor stimulus processing in

fatigue

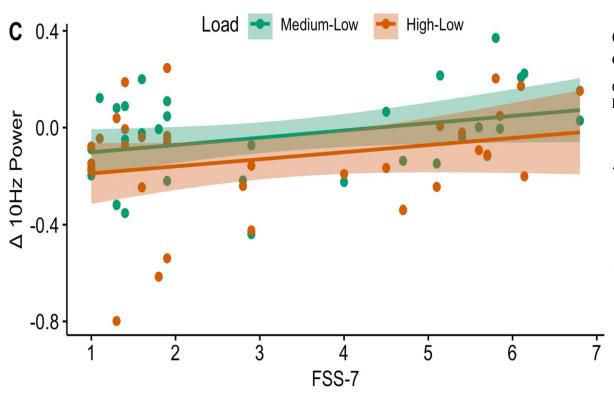
Clinical Neurophysiology 130 (2019) 692–700

Contents lists available at ScienceDirect

#### Clinical Neurophysiology

journal homepage: www.elsevier.com/locate/clinph

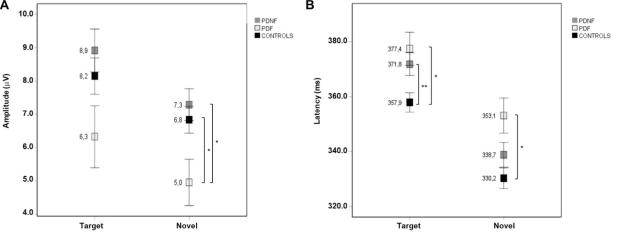




Central fatigue and attentional processing in Parkinson's disease: An event-related potentials study



Caterina Pauletti <sup>a,b,\*</sup>, Daniela Mannarelli <sup>a</sup>, Nicoletta Locuratolo <sup>a</sup>, Antonio Currà <sup>c</sup>, Lucio Marinelli <sup>d,e</sup>, Francesco Fattapposta <sup>a</sup>



Kuppuswamy et. al., 2021 in preparation

<u>Inability to switch attention from distractor to target</u> with increasing load explains fatigue

ORIGINAL ARTICLE



## **Abnormal Resting-State Neural Activity and Connectivity of Fatigue in Parkinson's Disease**

◆ Human Brain Mapping 38:283–292 (2017) ◆

Jie-Jin Zhang, Jian Ding, Jun-Yi Li, Min Wang, Yong-Sheng Yuan, Li Zhang, Si-Ming Jiang, Xi-Xi Wang, Lin Zhu<sup>1</sup> & Ke-Zhong Zhang<sup>1</sup>

1 Department of Neurology, The First Affiliated Hospital of Nanjing Medical University, Nanjing, China 2 Department of Radiology, The First Affiliated Hospital of Nanjing Medical University, Nanjing, China

## Fatigue in Parkinson's Disease: The Contribution of Cerebral Metabolic Changes

Sang Soo Cho, 1,2 Kelly Aminian, 1,2 Crystal Li,2 Anthony E. Lang,3 Sylvain Houle,<sup>2</sup> and Antonio P. Strafella<sup>1,2,3</sup>\*

## **OPEN** Post mTBI fatigue is associated with abnormal brain functional connectivity

September 2015

Love Engström Nordin<sup>1,2,\*</sup>, Marika Christina Möller<sup>3,4,\*</sup>, Per Julin<sup>3,5</sup>, Aniko Bartfai<sup>3</sup>, 18 January 2016 Farouk Hashim<sup>2,6</sup> & Tie-Qiang Li<sup>1,2</sup>

Fatigue is associated with abnormal activity in resting state salience networks

## Future directions

• Investigate reward prediction errors and sensory prediction errors in the context of trait fatigue and fatigability in disease.

 When investigating sensory attenuation – focus on all sensory inputs, not just somatosensory.

• When studying sensory perception, focus on proprioceptive, visual and auditory inputs, and multi-sensory integration.

# Acknowledgements

## The Effort Lab



Collaborators

Prof John Rothwell Prof Nilli Lavie Dr Lucie Charles Dr Anthony Harris Dr Katlyn Brown