

## **5 GENERAL DISCUSSION**

### **5.1 REFLECTIONS OF MAIN FINDINGS**

Fatigue is a frequently occurring, subjectively experienced, and complex phenomenon, present, not only as a common symptom of PPS and other diseases, but is also present in healthy individuals after mental and physical effort. Fatigue can originate in the central or peripheral nervous system or a combination of both. It can be related to stress, disordered sleep, infection and inflammatory processes, muscle overuse, anxiety, pain, disordered breathing, or high altitude and can be experienced in various ways, for example as general, mental, physical or muscle fatigue.

The present studies found that fatigued PPS patients had no particular cognitive difficulties compared with non-fatigued patients. They also were younger and had a lower QOL compared with the non-fatigued patients. The variance in Vitality was mostly explained by General fatigue, which in turn was mostly explained by physical variables and inversely correlated with age, i.e., older patients had a less fatigue. These findings indicate that most fatigue in PPS could be described as physical and not mental. A follow-up of IVIG treatment revealed several combinations of response patterns, i.e., positive, non- and negative responders, with Vitality, Bodily pain and Physical functioning as the outcome variables, in which the positive responders were more fatigued and had more pain than the non responders before treatment. The younger age and the more severe QOL, sleep and pain symptoms in the fatigued PPS patients, in combination with the existence of several response patterns, indicate that there may be subgroups of PPS patients.

#### **5.1.1 Do PPS patients experience cognitive difficulties?**

In study I, PPS patients were divided into groups according to whether or not they felt generally fatigued, and their cognition was assessed using neuropsychological tests. Mental fatigue was provoked by cognitive load. The results indicated no differences in tests performance between the fatigued and non-fatigued PPS patients and that there were load effects. The conclusion of study I was that fatigue did not affect cognitive performance in PPS patients. Other studies (Bruno et al. 1993, 1994, 1995, 2000) have found indications that PPS patients may have subtle cognitive difficulties with attention and word finding. The results of study I may indicate that the tests used were not sensitive enough, and the inclusion of a healthy control group might have supplied additional information helping to resolve the issue. However, the results may also

indicate that general fatigue in these groups, as seen in study II, can mostly be defined as physical fatigue. It may be that physical fatigue does not affect cognition in the same way as mental fatigue does. Further studies including normal controls would be needed to conclude that cognitive disturbances are present in PPS patients.

### **5.1.2 Physical fatigue: the most prominent fatigue type in PPS?**

In the large group of PPS patients examined in study II, the most prominent type of fatigue seemed to be physical fatigue. Variation in Vitality was explained by General fatigue which in turn was mainly explained by physical variables. It was therefore assumed that fatigue in PPS is primarily physical in nature. The findings of study II are confirmed by data from the studies by Trojan et al. (2004, 2009) and Schanke et al. (2001). However Bruno et al. (1994, 1995) suggested that brain-derived fatigue affects the subjective experience of fatigue in PPS. This assumption was based on abnormal CNS findings pertaining mainly to the reticular activating system (Bruno et al. 1994, 1995). The most severely fatigued group examined in study III, indeed suffered from mental fatigue, though even in this group, physical fatigue was primary and mental fatigue secondary. The results of the present studies, in accordance with data from other studies, point to that physical fatigue and not mental fatigue is the most prominent type of fatigue experienced by PPS patients.

### **5.1.3 Are there subgroups of fatigue in PPS?**

PPS is in itself a complex phenomenon, just like fatigue. PPS patients all have their own histories and individual courses of polio: some suffer from persistent paralysis or weaknesses, while others recover to an almost normal level. The number of affected muscles also differs between polio patients. The results of study III indicate a significant difference between fatigued and non-fatigued PPS patients in terms of age, QOL variables, pain levels and sleep quality, giving rise to different subgroups on the basis of these variables. The question is whether these differences result from fatigue level or whether they can be explained by other factors, such as the increased pain seen in the fatigued group. Study IV found several patterns of response to IVIG. One group of patients displayed a positive response in at least two outcome variables, i.e., Vitality and Bodily pain, another group displayed a negative response in both. This would indicate that there are different subgroups in this respect as well. PPS is thus not homogenous but is a heterogeneous condition with different subgroups. It would be of interest to further characterize these subgroups to evaluate the role of biological or contextual influences in defining them.

#### **5.1.4 Do all PPS patients benefit from IVIG treatment?**

Several studies, i.e., Kaponides et al. (2006), Gonzalez et al. (2006), and Farbu et al (2007), have identified a positive response to IVIG treatment in PPS patients, especially for the SF-36 subdomain of Vitality, and thus fatigue as well as pain. However, it was unclear whether all or just some patients experienced a positive response. The results of study IV indicate not only positive responses but the existence of several patterns of reaction to IVIG, i.e., positive, non-, and negative responders. Vitality was found to be a variable that may indicate a positive or negative treatment outcome. Effort should be made to further characterize responders, non-responders and negative responders, in order to offer treatment only to patients who will benefit from it and to avoid unnecessary treatment in patients who will not.

#### **5.1.5 Clinical implications**

Identifying the type of fatigue enables a more accurate focus in terms of treatment. The finding that fatigue is mostly physical in nature in PPS means that treatment and rehabilitation should focus on coping with and treatment of physical fatigue by saving energy, avoiding muscle disuse and overuse and physiotherapeutic interventions. However, in the most severely fatigued group, mental fatigue was present as well. It is important to lower the level of fatigue, since fatigue negatively affects QOL in general. Besides PPS related fatigue, PPS patients may, like everyone else, suffer from concomitant disorders having fatigue as a symptom and also be affected by “normal” fatigue: it is therefore important to thoroughly analyse the presented fatigue to be able to give the patient adequate care and therapy. Since the fatigued group examined in study III was younger, i.e., up to 65 years old, it is also important to into consider whether or not the patients’ work is physically demanding. More PPS patients in the fatigued group had contracted polio after 1956. The assumption was that this increased the possibility that they had contracted polio outside Sweden and might have a different contextual background – an aspect that may be important to take into consideration.

The results of the present studies indicate the existence of various subgroups of PPS patients and highlight the importance of using an individual approach when meeting a PPS patient. Taking contextual and emotional aspects into consideration may be important in helping these patients.

### 5.1.6 Future research

Several questions need to be answered concerning fatigue in PPS.

- To rule out cognitive dysfunction in PPS, a study including a group of healthy controls should be performed. The sample should be large enough and the presence of depression and other factors that can affect fatigue should be considered.
- The fatigued polio patients were younger than the non-fatigued patients examined in studies II and III. The question is why. It may be important to consider contextual factors including the work situation. It is also important to determine whether objective fatigue, defined as muscle weakness, increases and whether subjective fatigue decreases with increasing age.
- More of the fatigued patients had contracted polio after the introduction of polio vaccine in Sweden, i.e., after 1956. Do PPS patients who contracted polio before and after 1956 differ in terms of PPS related symptoms, QOL, mental health, family, and work situation?
- Connecting subjective QOL variables to biological parameters is another task for future research. Today we lack knowledge how the most common symptoms of PPS, i.e., muscle weakness, fatigue and pain, are related to inflammatory processes or other biomarkers.
- It is important to identify positive and negative responders before administering IVIG treatment. There may be factors, both in the background and contextual as well as the biological level that distinguish these different type of patients.
- PPS patients who had received more than one IVIG treatment were excluded from the sample. Finding out more about the effects of repeated IVIG treatment would be of interest. Would positive responders continue to be positive responders?
- Finding alternative treatment options, other than IVIG, for the negative and non-responders is another aim of future research.

## **6 SUMMARY AND CONCLUSIONS**

### **6.1 CONCLUSIONS REGARDING MAIN FINDINGS**

- There was no evidence that general fatigue or cognitive load affected cognitive functioning in PPS. No cognitive performance differences could be detected and systematic varying of test order did not cause significantly brain/mental fatigue.
- Vitality in PPS patients depends on physiological parameters. Mental fatigue is not a prominent predictor.
- Contrary to general belief, increasing vitality is correlated while pain is inversely correlated with increasing age in PPS patients.
- Fatigued PPS patients may be considered as a subgroup of PPS patients, characterized by significant lower age, more physical problems and lower QOL than non-fatigued PPS patients.
- In fatigued PPS patients mental fatigue was of relatively more importance for vitality than was physical fatigue.
- After IVIG treatment the total sample of PPS patients had significantly higher scores for the SF-36 sub-domains of Vitality, Bodily pain, Social functioning, Role-emotional and for MCS at the six-month follow-up than before treatment.
- The SF-36 sub-domains Vitality and Bodily pain may serve as outcome variables for IVIG treatment.
- PPS patients with low Vitality and Bodily pain scores may benefit from IVIG treatment while patients with higher scores may not.