



c.c. PCA
for Prof NG 2TB
Bial process
PCA
05. JUL. 2004

Fundação Bial, Instituição de utilidade pública
À Av. da Siderurgia Nacional
4785 S. Mamede do Coronado
Portugal

Your ref:

Our ref:

Date 30.06.04

SCIENTIFIC AND FINANCIAL PROGRESS REPORT FOR GRANT 28/02 TO PROFESSOR MAGNE ARVE FLATEN

Scientific progress report: A total of 4 experiments were planned. Experiment 1 started in April 2003 and was completed in March 2004. A total of 84 subjects were run, as planned. The study went very well and the preliminary data analyses show a clear-cut placebo effect. How this related to emotional and cognitive factors will be analysed in the fall of 2004.

Experiment 4 started in the summer of 2003 and is now completed. We have not yet done the data analyses.


We plan to start Experiment 2 in the fall of 2004.

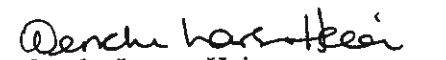
All in all the scientific progress is as planned, even a little ahead of time.

Financial progress report: No funds were used for 2003, since the cortisol and beta-endorphin analyses will be carried out after the completion of Experiments 1 and 4, and since no scientific assistant was hired for these two experiments. The funding for 2003 will instead be used in 2004-2005.

Please contact us if there are any questions.

Yours sincerely


Magne Arve Flaten, Professor PhD


Wenche Larsen Heia
Executive Economy Administrator

Administration

Faculty of social science

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Wenche Larsen Heia, telephone extension +47 46437, electronic mail: wenche@sv.uit.no



Bial PCA
20. APR. 2005

Bial Foundation
À. Av. da Siderurgia Nacional
4745-457 S. Mamede do Coronado Portugal
Porto, Portugal

Your ref: SCIENTIFIC PROGRESS REPORT FOR PROJECT 28/02

Our ref:

Date: 18.04.05

Dear Sirs,

This is the scientific progress report for Project 28/02 "Emotional factors in placebo analgesia: Psychophysiological experiments" led by Professor Dr. Magne Arve Flaten that you are referring to in your letter of April 12 2005.

Some information regarding the scientific progress of the project was sent you in my letter of March 31. In addition, I am now enclosing the manuscripts and other materials that we have produced based on the experiments supported by the Bial Foundation, together with statements regarding the progress of the project.

M.A. Flaten, P.-M. Aslaksen, A. Finset, T. Simonsen, O. Johansen (in preparation).
Cognitive and emotional factors in placebo analgesia.

This manuscript is based on Experiment 1 in the grant application. The ms will be sent to *Pain* for publication within 1-2 weeks. The experiment investigated whether cognitive factors (expectancies for drug effects) or emotional support was the strongest contributor to analgesia. We found that both processes reduced pain to the same amount, but the onset of the analgesia was different. The cognitive effect was seen at 5 minutes after pain induction, whereas the emotional effect was seen at about 40 minutes after pain induction. Surprisingly, the analgesic effect of emotional support was not mediated via changes in stress or negative emotions. Thus, cognitive factors were involved and seems to have played the most important role.

O. Friberg, O. Hjemdal, J.H. Rosenvinge, M.M. Martinussen, P.-M. Aslaksen, M.A. Flaten (submitted). Resilience as a modulator of pain and stress. This manuscript is based on Experiment 1 in the grant application, and has been submitted to *Psychosomatic Medicine* for publication. In this study, personality factors related to resilience were recorded prior to the experiment, and were correlated with ratings of pain, stress, and analgesia. The factor of social support, one important factor in the resilience construct, predicted analgesia. This means that individuals high in social support reported less pain. The magnitude of the effect was large, over 20 mm on the numerical rating scale, and clinically relevant.

P.-M. Aslaksen, M.A. Flaten (in preparation). Pain report is altered by social factors. This manuscript is based on Experiment 3 in the grant application. An abstract will be submitted to the meeting of the Society for Neuroscience in November 2005, and the manuscript will

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be submitted to *Pain* later this year, probably in the fall. We found in this experiment that the gender of the volunteer interacted with the gender of the experimenter. Thus, male volunteers displayed less pain when a female was the experimenter, and, more surprisingly, females displayed less pain when a male was the experimenter. Importantly, this was not related to emotional factors, so emotional factors previously shown to influence pain, did not play a role here. Thus, social factors seem to have influenced pain report and pain behaviour.

The empirical work in Experiment 4 in the grant application, The role of expectancy in physical therapy of lower back pain, has been finished. Two groups of subjects with chronic pain, i.e. rheumatoid arthritis and fibromyalgia patients, received either treatment as usual with physiotherapy and medical treatment, and another group received treatment as usual plus information about the disease and its treatment to see if cognitive factors (knowledge and expectancy) could have any effects on the pain. The data have not yet been scored and statistically analysed, and this will be done in the summer of 2005. We expect to start writing the introduction of the manuscript this spring, do the analyses in the summer, and we should have the manuscript finished later this year. As of now, I unfortunately cannot give any details about the results of the study at the present time, but the data should be available for the next progress report.

At this time we are planning the last study in the grant proposal, Experiment 2, that we should be ready to run in the summer or fall 2005.

Thus, the status of Project 28/02 is as follows: Of the four planned experiments, three have been run. From Experiment 1 two manuscripts have been written. From Experiments 3 and 4 one report will be written from each experiment. Experiment 2 will be started within the next few months.

If you need more information please contact me at any time.

Yours sincerely



Magne Arve Flaten, Professor
Dr. Psychol.



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04. APR 5
BIAL PCA

Bial Foundation
À Av. da Siderurgia Nacional
4745-457 S. Mamede do Coronado Portugal
Porto, Portugal

Your ref:

Our ref:

Date: 31.03.05

PROGRESS REPORT PROJECT 28/02 IN THE BIAL FELLOWSHIP PROGRAMME,
"COGNITIVE AND EMOTIONAL FACTORS IN PLACEBO ANALGESIA:
PSYCHOPHYSIOLOGICAL EXPERIMENTS" AS OF MARCH 31 2005

First of all we express our apologies for being so late with the progress report. This is entirely our fault and we will make sure that it will not happen again. .

Scientific progress report: A total of 4 experiments were planned in the original project. Experiment 1 started in April 2003 and was completed in March 2004. The report from the study is now under consideration for publication in *Science*, and the data were presented in March 2005 at the meeting of the American Psychosomatic Society in Vancouver, and will also be presented at the meetings of the Society for Psychophysiological Research in Lisboa in September and the Society for Neuroscience in Washington D.C. in November 2005. Other portions of the data are under consideration for publication in the acknowledged journal *Annals of Behavioral Medicine*.

Experiment 4 started in the summer of 2003 and is completed. We expect to submit the report in the fall of 2005.

Experiment 2 was completed in February of 2005. The data have been analysed and we expect to submit the report to the acknowledged journal *Pain* in the fall of 2005. The data will also be presented at the meeting of the Neuroscience Society in Washington D.C. in November 2005.

As of now, we are preparing for running Experiment 3, the last in the series. We should be able to start running this summer (2005).

All in all the scientific progress is as planned, even a little ahead of time.

Financial progress report: See the enclosed copies of invoices. On the first page there is the rate of € to Norwegian Kroner (NOK).

The sum used since the last financial progress report is 12.144,70 € (100.061,40 NOK). The main portion of this relates to the β -endorphin analyses of Experiment 1: The assays from MD Biosciences were 12.768 Swiss Francs (67.971,72 NOK), and the VAT and other minor charges amounted to 17.625 NOK, plus a first assay that cost 680 Swiss Franc (3.628,68 NOK). Then there are two payments of patients relating to Experiment 4, each of 3.360 NOK, and one payment of equipment of 4.116 NOK.

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MD Biosciences assays	NOK 67.971,72
MD Biosciences assay	NOK 3.628,68
VAT, freight, other expenses relating to assays	NOK 17.625,-
Payment of patients (3.360NOK x 2)	NOK 6.720,-
<u>Equipment Hi-Fi Klubben</u>	<u>NOK 4.116,-</u>
Sum	NOK 100.061,40
Equivalent to € 12.144.70	

The second instalment of the grant from the Bial Foundation was 14.700€, and the remaining sum is transferred to the budget for 2005 (14.700€ – 12.144,70€ = 2.555,30€) (see below). We hope this is acceptable to the Bial Foundation.

Budget 2005

Assays for salivary cortisol Experiment 3	4.500€
Equipment and expenses related to instalment of equipment (e.g., cables, thermode, A/D converter, PC-equipment)	6.000€
Payment one assistant for Experiment 3	5.000€
Running expenses (e.g., electrodes, gel)	2.000€
Payment participants Experiment 3	1.000€
Travel expenses related to presentations of the research supported by the Bial Foundation:	
Society for Psychophysiological Research meeting, Lisboa (9/05)	1.500€
Society for Neuroscience meeting, Washington DC (11/05)	2.500€
<u>Sum</u>	<u>22.500€</u>

Magne Arve Flaten
Magne Arve Flaten
Professor Dr. Psychol.
Principal Investigator

W. Larsen Heia
Wenche Larsen Heia
Officer of the Economy Unit

Tromsø March 31 2005



c.c.RCA

Bial Foundation
À. Av. da Siderurgia Nacional
4745-457 S. Mamede do Coronado Portugal
Porto, Portugal

Your ref:

Our ref:

Date: 31.01.2006

PROGRESS REPORT FOR PROJECT 28/02 FOR 2005/2006

Dear Sirs,

This is the progress report for Project 28/02 "Emotional factors in placebo analgesia: Psychophysiological experiments" led by Professor Dr. Magne Arve Flaten, for the period 18.04.2005, when the last progress report was sent, to 31.01.2006.

The manuscripts that we have produced based on the experiments supported by the Bial Foundation listed below, together with a statement regarding the progress of the project (below).

The status of Project 28/02 is as follows: Four experiments were planned. Three experiments have been run, and the running of the final experiment will be finished in March 2006. From Experiment 1 two manuscripts are in press in an international journal of good reputation (the impact factor of the *Journal of Psychosomatic Research* was 2.8 in 2004). Data from Experiment 2 have been presented at a scientific conference and the manuscript is under review in a scientific journal. From the other two experiments one report will be written from each experiment.

The following reports are in press:

M.A. Flaten, P.M. Aslaksen, A. Finset, T. Simonsen, O. Johansen (*Journal of Psychosomatic Research*, in press). "Cognitive and emotional factors in placebo analgesia." This manuscript is based on Experiment 1 in the grant application. The ms will be sent to *Pain* for publication within 1-2 weeks. The experiment investigated whether cognitive factors (expectancies for drug effects) or emotional support was the strongest contributor to analgesia. We found that both processes reduced pain to the same amount, but the onset of the analgesia was different. The cognitive effect was seen at 5 minutes after pain induction, whereas the emotional effect was seen at about 40 minutes after pain induction. Surprisingly, the analgesic effect of emotional support was not mediated via changes in stress or negative emotions. Thus, cognitive factors were involved and seems to have played the most important role.

O. Friberg, O. Hjemdal, J.H. Rosenvinge, M. Martinussen, P.M. Aslaksen, M.A. Flaten (*Journal of Psychosomatic Research*, in press). "Resilience as a modulator of pain and stress." This manuscript is based on Experiment 1 in the grant application, and has been submitted to *Psychosomatic Medicine* for publication. In this study, personality factors related to resilience were recorded prior to the experiment, and were correlated with ratings

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of pain, stress, and analgesia. The factor of social support, one important factor in the resilience construct, predicted analgesia. This means that individuals high in social support reported less pain. The magnitude of the effect was large, over 20 mm on the numerical rating scale, and clinically relevant.

The following report has been submitted to a scientific journal:

P.M. Aslaksen, M.A. Flaten (submitted). "Interaction of experimenter gender and participant gender in pain report." This manuscript is based on Experiment 3 in the grant application. A poster was presented at the meeting of the Society for Neuroscience in Washington, D.C. in November 2005. Findings from this experiment was that the gender of the volunteer interacted with the gender of the experimenter. Thus, male volunteers displayed less pain when a female was the experimenter, and, more surprisingly, females displayed less pain when a male was the experimenter. Importantly, this was not related to emotional factors, so emotional factors previously shown to influence pain, did not play a role here. Thus, social factors seem to have influenced pain report and pain behaviour.

The following reports are being prepared:

P.M. Aslaksen, M.A. Flaten (in preparation). "Classical conditioning of pain. Subjective and psychophysiological responses." Based on Experiment 2 in the grant application. So far about 50 of a total of 64 subjects have been run. The study will be presented at the meeting of the Society for Neuroscience and the Society for Psychophysiological Research in October 2006, and will be submitted to *Pain* this year. The data from this study will be presented at the Bial symposium in March 2006.

O. Johansen, M.A. Flaten (in preparation). "The role of symptom-related information on treatment of fibromyalgia and low-back pain" The empirical work in Experiment 4 in the grant application has been finished. Two groups of subjects with chronic pain, i.e. rheumatoid arthritis and fibromyalgia patients, received either treatment as usual with physical therapy and medical treatment, and another group received treatment as usual plus information about the disease and its treatment to see if cognitive factors (knowledge and expectancy) could have any effects on the pain. We expect to submit the manuscript this spring.

PUBLICATIONS FROM THE PROJECT AS OF JANUARY 2006

Publications in journals with peer review

Flaten, M.A., Aslaksen, P.M., Simonsen, T., Finset, A., & Johansen, O. Cognitive and emotional factors in placebo analgesia. *Journal of Psychosomatic Research*, in press

Friborg, O., Hjemdal, O., Rosenvinge, J.H., Martinussen, M., Aslaksen, P.M., & Flaten, M.A. Resilience as a modulator of pain and stress. *Journal of Psychosomatic Research*, in press

Planned publications

Aslaksen, P.M., Flaten, M.A. Interaction of experimenter gender and participant gender in pain report. *European Journal of Pain*.

Aslaksen, P.M., Flaten, M.A. Classical conditioning of pain. Subjective and psychophysiological responses. Will be submitted to *Pain*.

Johansen, O., Flaten, M.A. The role of symptom-related information on treatment of fibromyalgia and low-back pain. Will be submitted to the *European Journal of Pain*.

Conference presentations

Friborg, O., Hjemdal, O., Martinussen, M., Rosenvinge, J., Flaten, M.A., & Aslaksen, P.M. (2004). Social competence: Maybe the best predictor of resilience? 28th International Congress in Psychology Conference, Beijing, 12-15/6.

Finset, A., Aslaksen, P.M., Simonsen, T., Johansen, O., & Flaten, M.A. (2005). The effect of stress and information on pain and placebo analgesia. Meeting of the American Psychosomatic Society, Vancouver, Canada, 25-28/3.

Finset, A., Aslaksen, P.M., Simonsen, T., Johansen, O., & Flaten, M.A. (2005). Effects of drug-related information and support on placebo analgesia. International College of Psychosomatic Medicine meeting, Kobe, Japan, 21-26/8.

Flaten, M.A., Aslaksen, P.M., Simonsen, T., Finset, A., & Johansen, O. (2005). Cognitive and emotional factors in placebo analgesia. Meeting of the Society for Psychophysiological Research, Lisboa, Portugal, 22-25/9.

Aslaksen, P.M., Simonsen, T., Finset, A., Johansen, O., & Flaten, M.A. (2005).

Information about drug and information about pain both reduce perceived pain. Society for Neuroscience meeting, Washington, D.C., 12-16/11.

Flaten, M.A., Aslaksen, P.M., Simonsen, T., Finset, A., & Johansen, O. (2005). Emotional processes are not involved in placebo analgesia. Society for Neuroscience meeting, Washington, D.C., 12-16/11.

Aslaksen, M.A., Flaten, M.A. (2006). Classical conditioning modulates pain. Society for Neuroscience meeting, Atlanta, GA, 14-18/10.

Aslaksen, M.A., Flaten, M.A. (2006). The role of classical conditioning in modulation of pain report by social factors. Society for Psychophysiological Research meeting, Vancouver, Canada, 24-28/10.

FINANCIAL REPORT OF PROJECT 28/02

The rate of Norwegian Kroner (NOK) to Euro has been set at 8.11/1 which is today's exchange rate.

Budget 2005:

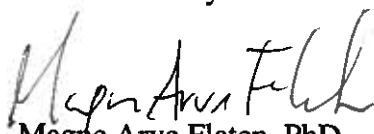
Transferred from the 2004 budget= €2.555,30. Bial transfer for 2005 = €14.700. Total amount for use in 2005 = €17.255,30 (NOK 139.940,48)

Account (T)	Amount in NOK
Customs and spedition charges	31 838,68
Scientific equipment	16 682,76
Data equipment	18 840,00
Laboratory equipment	3 707,00
Books	2 928,00
Other equipment	1 112,24
Office, running costs	495,00
Printing charges, reprints	2 675,21
Travel scientific conferences	34 518,96
Conference fees	2 488,10
Membership scientific organizations	2 254,19
Laboratory insurance costs	2 179,00
Other	4 032,16
Sum	123 751,30

We ask that the remaining sum in the 2005 budget, NOK 16.189,18 (€1996,20), is transferred to 2006, and should be used for Dr. Flaten's travel to the Bial Symposium in March 2006. The Economy Administrator will send you the final report in October 2006.

If you need more information please contact me at any time.

Yours sincerely


Magne Arve Flaten, PhD
Professor


Wenche Larsen Heia
Executive Economy Administrator

Tromsø, 31.01.2006



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Prof. Prof. NG
D.D.F. el
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PCA

16. OUT. 2006

Bial Foundation
À. Av. da Siderurgia Nacional
4745-457 S. Mamede do Coronado Portugal
Porto, Portugal

Your ref:

Our ref:

Date: 12.10.2006

THE VERY FINAL PROGRESS REPORT FOR PROJECT 28/02

Dear Sirs,

This is the very final progress report for Project 28/02 "Emotional factors in placebo analgesia: Psychophysiological experiments" led by Professor Dr. Magne Arve Flaten, The previous final progress report was sent to you on 06.06.2006, and in that report we asked that the unused sum of NOK 16.189,18 (€1996,20) could be used for expenses in 2006. In that report the scientific progress of the project was summarised and you asked for documentation of expenses in that report. This documentation, i.e., certified copies of expenses, is enclosed in the present report.

Furthermore, to receive the final 4900€ that was granted you asked us in your letter of 12th September 2006 for the certified copies of expenses, together with a final scientific report. The budget below specifies and documents expenses relating to the sum of (€1996,20 + €4900,-) €6896,20, equivalent to NOK 58617,70.

Account status pr. 12.10.2006 - prosjekt A3319 - Bial

Account		Period	Sum (NOK)
7152	Travel – Porto	200604	13 472,62
5013	Salary, scientific assistance	200605	4 223,52
5411	Tax, salary, scientific assistance	200605	595,51
6524	Data equipment	200606	4 298,00
	Data equipment	200606	13 842,50
	Data equipment	200606	730,83
	Data equipment	200606	10 698,75
	IT-services	200606	729,00
	Various expenses	200606	591,00
	Various expenses	200606	3 572,14
	Travel – Budapest, Scientific meeting	200606	14 419,58
	Sum		67 173,45

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SCIENTIFIC REPORT OF PROJECT 28/02

PUBLICATIONS FROM THE PROJECT AS OF JANUARY 2006

Publications in journals with peer review

- Flaten, M.A., Aslaksen, P.M., Simonsen, T., Finset, A., & Johansen, O. (2006). Cognitive and emotional factors in placebo analgesia. *Journal of Psychosomatic Research*, *61*, 81-89.
- Friborg, O., Hjemdal, O., Rosenvinge, J.H., Martinussen, M., Aslaksen, P.M., & Flaten (2006). M.A. Resilience as a modulator of pain and stress. *Journal of Psychosomatic Research*, *61*, 213-219.

Under review

- Aslaksen, P.M. & Flaten, M.A. Autonomic and subjective pain responses in the presence of male and female experimenters. Under review in *Pain*.

Planned publications

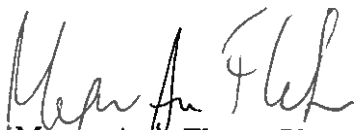
- Aslaksen, P.M., Flaten, M.A. Interaction of experimenter gender and participant gender in pain report. *European Journal of Pain*.
- Aslaksen, P.M., Flaten, M.A. Classical conditioning of pain. Subjective and psychophysiological responses. Will be submitted to *Pain*.
- Johansen, O., Flaten, M.A. The role of symptom-related information on treatment of fibromyalgia and low-back pain. Will be submitted to the *European Journal of Pain*.

Conference presentations

- Friborg, O., Hjemdal, O., Martinussen, M., Rosenvinge, J., Flaten, M.A., & Aslaksen, P.M. (2004). Social competence: Maybe the best predictor of resilience? 28th International Congress in Psychology Conference, Beijing, 12-15/6.
- Finset, A., Aslaksen, P.M., Simonsen, T., Johansen, O., & Flaten, M.A. (2005). The effect of stress and information on pain and placebo analgesia. Meeting of the American Psychosomatic Society, Vancouver, Canada, 25-28/3.
- Finset, A., Aslaksen, P.M., Simonsen, T., Johansen, O., & Flaten, M.A. (2005). Effects of drug-related information and support on placebo analgesia. International College of Psychosomatic Medicine meeting, Kobe, Japan, 21-26/8.
- Flaten, M.A., Aslaksen, P.M., Simonsen, T., Finset, A., & Johansen, O. (2005). Cognitive and emotional factors in placebo analgesia. Meeting of the Society for Psychophysiological Research, Lisboa, Portugal, 22-25/9.
- Aslaksen, P.M., Simonsen, T., Finset, A., Johansen, O., & Flaten, M.A. (2005). Information about drug and information about pain both reduce perceived pain. Society for Neuroscience meeting, Washington, D.C., 12-16/11.
- Flaten, M.A., Aslaksen, P.M., Simonsen, T., Finset, A., & Johansen, O. (2005). Emotional processes are not involved in placebo analgesia. Society for Neuroscience meeting, Washington, D.C., 12-16/11.
- Aslaksen, M.A., Flaten, M.A. (2006). Classical conditioning modulates pain. Society for Neuroscience meeting, Atlanta, GA, 14-18/10.
- Aslaksen, M.A., Flaten, M.A. (2006). The role of classical conditioning in modulation of pain report by social factors. Society for Psychophysiological Research meeting, Vancouver, Canada, 24-28/10.
- Aslaksen, M.A., Flaten, M.A. (2006). The role of classical conditioning in pain. Health Research Conference for North Norway, Tromsø, Norway, 1-2/11.
- Aslaksen, M.A., Flaten, M.A. (2007). The role of stress in placebo analgesia. Meeting of the American Psychosomatic Society, Budapest, Hungary, 7-10/3.

If you need more information please contact me at any time.
Finally, we would like to thank the Bial Foundation for their generous support of our research,
and for the inspiring conferences held in Porto.

Yours sincerely



Magne Arve Flaten, PhD
Professor



Wenche Larsen Heia
Executive Economy Administrator

Tromsø, 12.10.2006