Research findings in “Chemo-brain”

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Outline

- Background

- Our preliminary results:
  - Cognitive functioning in Post-treatment patients
  - Cognitive functioning in Pre-treatment patients
  - Psycho-social functioning

- Future directions
Effect of chemotherapy on cognitive functioning
Effect of chemotherapy on cognitive functioning
Effect of chemotherapy on cognitive functioning
Effect of chemotherapy on cognitive functioning
Chemo-brain

No central nervous system treatments

No brain tumours
Chemo-brain

No central nervous system treatments

No cranial irradiation

No brain tumours
Chemo-brain

Everyone?
Chemo-brain

Everyone?

Risk factors?
Chemo-brain

Everyone?

Temporary? Long lasting?

Risk factors?
Everyone?

Temporary? Long lasting?

Risk factors?
Chemo-brain

- Everyone?
- Before chemotherapy?
- Temporary? Long lasting?
- Risk factors?
Everyone?

Before chemotherapy?

Chemotherapy? Hormones? Corticosteroids? Anxiety/Depression/Tiredness?

Temporary? Long lasting?

Risk factors?
Paediatric patients

Mean age = 10

Krull et al., *JCO*, 2013
Paediatric patients

Mean age = 10

Acute lymphoblastic leukaemia

Krull et al., *JCO*, 2013
Paediatric patients

Acute lymphoblastic leukaemia

Mean age = 10

Wilms’ tumour

Krull et al., JCO, 2013
Paediatric patients

Acute lymphoblastic leukaemia
29-59% impaired

Mean age = 10

Wilms’ tumour

Krull et al., JCO, 2013
Adult patients

Mean age = 55
Adult patients

Breast cancer

Mean age = 55
Adult patients

Mean age = 55

Breast cancer

Testicular cancer
Adult patients

Mean age = 55

Breast cancer

Testicular cancer

Other: lung, colorectal, lymphoma
Adult patients

Mean age = 55

Breast cancer

Testicular cancer

Up to 80% complain of poor cognitive performance

Other: lung, colorectal, lymphoma

Mean age = 55
Our group

16-50 year old patients
Our group

Lymphoma

16-50 year old patients
Our group

Lymphoma

Sarcoma

16-50 year old patients
Our group

- Lymphoma
- Sarcoma
- Germ cell tumour
- 16-50 year old patients
16-50 year old patients

- Lymphoma
- Sarcoma
- Germ cell tumour
- Breast cancer
Our group

Before treatment
N=30

After treatment
N=75

Control
N=96
Our group

Before treatment  
N=30

After treatment  
N=75

Control  
N=96

Effects?  
Which ones?  
Other factors?
12 neuropsychological tests: attention, memory, planning/self-monitoring.

Psycho-social questionnaires: cognitive complaints, symptoms, anxiety, depression, tiredness, quality of life.
- 75 patients versus 75 healthy matched controls
- 6 months to 5 years post-treatment (mean=2.5 years)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Survivors</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (m/sd)</td>
<td>35.55 (9.49)</td>
<td>29.62 (9.84)</td>
</tr>
<tr>
<td>Sex (m/sd)</td>
<td>0.48 (0.50)</td>
<td>0.53 (0.50)</td>
</tr>
<tr>
<td>Years of education (m/sd)</td>
<td>14.20 (2.22)</td>
<td>15.15 (2.14)</td>
</tr>
</tbody>
</table>
Post-treatment patients

Survivors - cancer type

- Hodgkin’s lymphoma: 17
- Non-Hodgkin lymphoma: 15
- Breast cancer: 16
- Germ cell tumour: 17
- Sarcoma: 10
Results
Post-treatment patients

Average

50% below 50% above

Percentile Scores
Results
Post-treatment patients

30% below  Slightly lower  70% above
Results
Post-treatment patients

Very low

90% above
Remembering a story:

“On Wednesday afternoon/ Mr. Jones was waiting for his train/ in the local station/. The train was delayed/ and he had to wait for an additional 20 minutes. “
Verbal memory
Post-treatment patients

<table>
<thead>
<tr>
<th>Test</th>
<th>Post-treatment</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Story immediate recall</td>
<td>22%</td>
<td>8%</td>
</tr>
<tr>
<td>Story delayed recall</td>
<td>24%</td>
<td>7%</td>
</tr>
</tbody>
</table>
Verbal memory
Post-treatment patients

Percentage participants

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**p<.01
Recognising two lists of words

List A
Dog
Plate
Pencil
Skate

Read and recall 5 times
Recognising two lists of words

- **List A**
  - Dog
  - Plate
  - Pencil
  - Skate
  - Read and recall 5 times

- **List B**
  - Pigeon
  - Book
  - Sand
  - Mug
  - Read and recall once
Recognising two lists of words

<table>
<thead>
<tr>
<th>List A</th>
<th>List B</th>
<th>List A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dog</td>
<td>Pigeon</td>
<td>?</td>
</tr>
<tr>
<td>Plate</td>
<td>Book</td>
<td>Read and recall</td>
</tr>
<tr>
<td>Pencil</td>
<td>Sand</td>
<td>once</td>
</tr>
<tr>
<td>Skate</td>
<td>Mug</td>
<td>Recall</td>
</tr>
</tbody>
</table>

Read and recall 5 times

Read and recall once
**Verbal memory**

Post-treatment patients

- Recognising two lists of words

<table>
<thead>
<tr>
<th>List A</th>
<th>List B</th>
<th>List A</th>
<th>Recall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dog</td>
<td>Pigeon</td>
<td>Dog</td>
<td></td>
</tr>
<tr>
<td>Plate</td>
<td>Book</td>
<td>Horse</td>
<td></td>
</tr>
<tr>
<td>Pencil</td>
<td>Sand</td>
<td>Paper</td>
<td></td>
</tr>
<tr>
<td>Skate</td>
<td>Mug</td>
<td>Phone</td>
<td></td>
</tr>
</tbody>
</table>

- Which word? From which list?

<table>
<thead>
<tr>
<th>Dog</th>
<th>Horse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paper</td>
<td>Sand</td>
</tr>
<tr>
<td>Phone</td>
<td>Skate</td>
</tr>
<tr>
<td>Pigeon</td>
<td>Train</td>
</tr>
<tr>
<td>Rabbit</td>
<td>Plate</td>
</tr>
<tr>
<td>Mug</td>
<td>Apple</td>
</tr>
<tr>
<td>Pencil</td>
<td>Guitar</td>
</tr>
<tr>
<td>Kettle</td>
<td>Book</td>
</tr>
</tbody>
</table>
Recognising two lists of words

List A
- Dog
- Plate
- Pencil
- Skate

Read and recall 5 times

List B
- Pigeon
- Book
- Sand
- Mug

Read and recall once

List A
- ?

Recall

Which word? From which list?

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<tr>
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<td>Pencil</td>
<td>Guitar</td>
</tr>
<tr>
<td>Kettle</td>
<td>Book</td>
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</tbody>
</table>
Verbal memory
Post-treatment patients

Percentage participants

Test

A words
B words
Word recognition
Source: List A
Source: List B
List recognition

21%
47%
45%
14%
15%
14%
10%
14%
14%
2%
9%
4%
32%
39%
Verbal memory
Post-treatment patients

- A words: 21%
- B words: 14%
- Word recognition: 14%
- Source: List A: 15%
- Source: List B: 9%
- List recognition: 4%

- Post-treatment: 47%
- Controls: 10%

*p < .01*
Visuo-spatial abilities
Post-treatment patients

Percentage participants

Post-treatment: 79%
Controls: 53%

Group

Post-treatment
Controls

Post-treatment
Controls

NHS
NHS Foundation Trust
The Christie
The University of Manchester
**Visuo-spatial abilities**

Post-treatment patients

**< .001

<table>
<thead>
<tr>
<th>Group</th>
<th>Percentage participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-treatment</td>
<td>79%</td>
</tr>
<tr>
<td>Controls</td>
<td>53%</td>
</tr>
</tbody>
</table>

**$**
30 pre-treatment patients versus 30 healthy matched controls

<table>
<thead>
<tr>
<th>Variable</th>
<th>New patients</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (m/SD)</td>
<td>30.92 (13.01)</td>
<td>30.57 (12.38)</td>
</tr>
<tr>
<td>Sex (m/SD)</td>
<td>0.71 (0.46)</td>
<td>0.67 (0.47)</td>
</tr>
<tr>
<td>Years of education (m/SD)</td>
<td>13.57 (1.81)</td>
<td>14.96 (2.65)</td>
</tr>
</tbody>
</table>
Pre-treatment patients

- Hodgkin: 8 patients
- Non-Hodgkin: 1 patient
- Breast cancer: 12 patients
- Germ cell tumour: 2 patients
- Sarcoma: 7 patients
Attention
Pre-treatment patients
Attention
Pre-treatment patients

<table>
<thead>
<tr>
<th>Group</th>
<th>Percentage participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-treatment</td>
<td>7%</td>
</tr>
<tr>
<td>Controls</td>
<td>1%</td>
</tr>
</tbody>
</table>
Attention
Pre-treatment patients

**p<.01
Visuo-spatial abilities
Pre-treatment patients

**Pre-treatment controls**

<table>
<thead>
<tr>
<th>Group</th>
<th>Percentage participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-treatment</td>
<td>68%</td>
</tr>
<tr>
<td>Controls</td>
<td>53%</td>
</tr>
</tbody>
</table>

**Legend:**
- Orange: Pre-treatment
- Blue: Controls
Visuo-spatial abilities
Post-treatment patients

**p<.01

**
Quality of life

![Bar chart showing quality of life pre-treatment, post-treatment, and control.](chart.png)

**p < .001**
Symptoms

<table>
<thead>
<tr>
<th></th>
<th>Pre-treatment</th>
<th>Post-treatment</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms</td>
<td>19</td>
<td>27</td>
<td>7</td>
</tr>
<tr>
<td>Cognitive complaints</td>
<td><strong>41</strong></td>
<td><strong>46</strong></td>
<td><strong>34</strong></td>
</tr>
</tbody>
</table>

**p<.001
Distress and tiredness

- Anxiety: Pre-treatment 8, Controls 6
- Depression: Pre-treatment 9, Controls 5, Post-treatment 4
- Tiredness: Pre-treatment 16, Post-treatment 16, Controls 13

The Christie NHS Foundation Trust
Influence on cognition
Pre-treatment patients

Symptoms
- Tiredness
- Depression
- Cognitive complaints

5-9 % change

Attention
Influence on cognition
Post-treatment patients

Symptoms

up to 7% change

Attention

Anxiety
+Depression

3-20% change

Memory
Post-treatment patients - poor memory for verbal information and find it difficult to represent visuo-spatial information.

Pre-treatment patients - lower attention and poor performance on visuo-spatial tests.

All patients - lower psycho-social functioning.

They explain a part, but not all of the cognitive issues.
Future directions

- More research on potential mechanisms
Future directions

- More research on potential mechanisms
- To inform potential treatments
Future directions

- More research on potential mechanisms
- To inform potential treatments
Future directions

- More research on potential mechanisms
- To inform potential treatments

Physical exercise ?
Future directions

- Clinical trials
Future directions

- Clinical trials
- Extend to imaging studies
Future directions

- Clinical trials
- Extend to imaging studies
- And translational studies
Thank you for your attention!
 Acknowledgements

- All the participants who took part in our study
- The Medical Research Council for funding this project
- My supervisors: Dr. Martin McCabe, Prof. Andrew Mayes, Prof. Alison Wearden, and Dr. Deborah Talmi
- My advisor: Prof. Linda McGowan
- The clinical teams and research nurses in the 5 NHS Trusts: Prof. John Radford, Dr. Kim Linton, Dr. Adam Gibson, Dr. Goode, Dr. Welch, Dr. Kalakonda, Dr. Leahy,
- Students who contributed to this work.