A comprehensive analysis of chemotherapy-induced cognitive changes

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BACKGROUND

Studies with animals
- Impaired functions: spatial memory, object and location learning, fear conditioning, and reward learning;
- Affected structures: hippocampus, subventricular zone, corpus callosum; dendritic swelling, cell death, reduced proliferation;
- Limitations: Healthy animals with no malignancies.

Studies with adults
- Impaired functions: memory, attention, executive functions, speed of processing, motor functions;
- Affected structures: frontal, parietal, temporal, cerebellar regions; decreased white and grey matter from 1 to 10 years post-treatment;
- Limitations: women with breast cancer and more recently men with testicular cancer.

Studies with children
- Impaired functions: full scale IQ, verbal IQ, performance IQ, memory, attention, executive functions;
- Limitations: lack of longitudinal designs, children with acute lymphoblastic leukaemia (CNS-directed therapy), different constructs, no assessments of fatigue and distress.

OBJECTIVES
- Identify the similarities and differences between the three lines of research;
- To inform future directions of research in the field.

METHODOLOGY

Study selection process:
- Databases: PubMed, Psychinfo, ICCTF and IPOS conference proceedings, between the earliest date (1980) and January 2012;
- Inclusion/ exclusion criteria based on ICCTF guidelines;
- Study quality analysis (Downs and Black (1998) scale: 6 scales, 34 items);
- Inclusion/ exclusion criteria based on ICCTF guidelines;
- Full copies obtained and assessed for eligibility (353);
- Excluded (621); Studies from reference lists (81);
- Excluded (226) Irrelevant outcome (216) Duplicate publications (10);
- Insufficient data (31);
- Study quality analysis (Downs and Black (1998) scale: 6 scales, 34 items);
- Complex data structures: subgroup analyses based on study designs;
- Effect size is Hedges g; heterogeneity is I², unadjusted p < 0.05;
- Random-effects meta-analysis.

RESULTS

Studies with animals
- Escape latency in Morris Water Maze: Effect size (ES)=-0.42 (-1.08 to 0.23);
- Object and place recognition;
- Exploration time ES=-0.45 (-0.82 to -0.08);
- Location/object preference and avoidance tasks: not significant.

Studies with adults
- Controls versus Patients at Baseline, Controls versus Patients at Follow-up, Patients at baseline versus follow-up, Controls at baseline versus follow-up;
- Heterogeneity is under 0.85 for all the marked constructs (■);
- Five or less studies for all the marked constructs or groups (▲).

CONCLUSIONS

- Spatial and object /place recognition impaired in animals, but not conditioning;
- Clinicians should be sensitive to:
  - Impairments in delayed, recognition, verbal memory, attention, and visuospatial functions impaired in adults and children;
  - Subjective complaints regarding memory and attention/executive functions in up to 42% of cancer patients.
- Heterogeneity is very high and influenced by: study quality, study designs, tests included in constructs;
- Longitudinal assessments of the same patients show improvements compared to single time assessments - false positive and practice effects.

Studies with children
- When available, longitudinal patient assessments positive and high effect sizes (memory and visual memory);
- No evaluation of distress and fatigue.

Fig 1 Chemotherapy effects on adult cognitive functioning
Fig 2 Chemotherapy effects on adult memory functioning
Fig 3 Distress effects on cognition
Fig 4 Chemotherapy effects on child cognitive functioning
Fig 5 Chemotherapy effects on child memory and attention