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# Potential direct neuropsychiatric effects:

Psychiatric illnesses, such as depression and anxiety are common, but often neglected, complications of cancer. These most commonly arise from a patient's psychological reactions to diagnosis, treatment, relapse, end of life care, or survivorship. Direct biological effects of certain treatments and tumour types can also give rise to symptoms of depression or anxiety. These under-recognised, yet often reversible biological pathways are summarised below.

## Cancer treatments

### Cancer surgery

- Gastric surgery
  - Total gastrectomy
  - Ileal resection
- Bilateral oophorectomy
- Thyroidectomy
- Pancreatectomy
- Frontal lobe Neurosurgery

### Radiotherapy

- Head and neck
- Pelvic
- Whole brain

### Chemotherapeutic agents

- Mitotic spindle poisons
  - Paclitaxel
  - Vincristine
- Azacitidine
- Etoposide
- Antimetabolites
  - Methotrexate
  - Pemetrexed
- Bexarotene
- Procarbazine
- Cisplatin

### Molecularly targeted agents

- VEGFR or multiple TK inhibitors
  - Sunitinib
  - Pazopanib
  - Axitinib
  - Vandetanib
  - Regorafenib
- Buparlisib
- Bcr-Abl inhibitors
  - Imatinib
  - Dasatinib
  - Nilotinib
- Proteasome inhibitors
  - Bortezomib
  - Carfilzomib

### Monoclonal antibodies

- Checkpoint inhibitors
  - Ipilimumab
  - Nivolumab
  - Pembrolizumab
- EGFR inhibitors
  - Cetuximab
  - Panitumumab
- Alemtuzumab

### Hormone treatments

- Letrozole
- Corticosteroids
- Androgen deprivation
  - Goserelin
  - Buserelin
  - Leuprolide
  - Flutamide

Theoretical risk

## Specific tumours

### Brain

- Meningiomas, gliomas, or metastases
  - Frontal lobe involvement
  - Temporal lobe involvement
- Pituitary tumours
  - Secretory pathology
    - Pituitary adenoma (Cushing's Disease) secreting ACTH
    - Prolactinomas
    - Pan-hypopituitarism — Destructive pathology

### Parathyroid

- Parathyroid hormone overproduction

### Lung

- Carcinoid tumours of the bronchus
  - Carcinoid syndrome
  - Paraneoplastic endocrine syndrome
  - Pellagra
- Small cell lung cancer
  - Paraneoplastic Cushing's syndrome
  - Paraneoplastic SIADH
- Non small cell lung cancer
  - Paraneoplastic endocrine syndrome

### Pancreas

- Ductal adenocarcinoma
  - Interleukin-6 release

### Ovary

- Rare (in very advanced disease)
- Onconeural (anti-Yo) antibody-mediated paraneoplastic cerebellar degeneration
- Onconeural (anti-NMDA receptor) antibody-mediated limbic encephalitis

### Adrenal

- Cortical
- Phaeochromocytoma

### Testicular

- Paraneoplastic endocrine syndrome
- Onconeural (anti-Ma2) paraneoplastic syndrome

### Other

- Myeloma, breast, renal, gynaecological, sarcoma, head and neck cancers
- Hodgkin's lymphoma
- Prostate, skin, colorectal, leukaemias

Few neuropsychiatric effects

## Direct neuropsychiatric effects

- Depression
- Anxiety
- Mania
- Euphoria, insomnia, restlessness, hyperactivity, suicidal ideation
- Agitation
- Irritability
- Psychosis
- Dis-inhibition
- Blunted affect
- Mood swings
- Personality changes
- Impaired short term memory
- Halluc-inations
- Disorien-tation
- Onconeural (anti-Tr) antibody-mediated paraneoplastic cerebellar degeneration
- Cerebellar cognitive-affective syndrome
- Delirium
- Encephal-opathy
- Cognitive impairment
- Aggression
- Cushing's syndrome
  - Severe atypical depression
  - Hypersomnia
  - Hyperphagia
  - Sometimes with:
    - Visuospatial memory impairment
  - Delusions
- Executive function deficits
- Déjà vu
- Complex motor behavioural disturbance
- Gustatory and auditory hallucinations
- Expressive dysphasia
- Emotional lability
- Apathy
- Inadequate replacement of thyroid hormone
- Hypopara-thyroidism
- Pan-hypo-pituitarism
- Chronic oestrogen deficiency
- B12 deficiency
- Melatonin deficiency
- Insomnia
- TSH deficiency or gonadotrophin deficiency
- Mood disturbance
- Hypo-thyroidism
- Hypo-calcaemia
- Growth hormone deficiency
- Hyper-calcaemia
- Graves' disease
- Hyper-thyroidism

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