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‘Give-up-itis’ revisited: Neuropathology of *extremis*

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ABSTRACT

The term ‘give-up-itis’ describes people who respond to traumatic stress by developing extreme apathy, give up hope, relinquish the will to live and die, despite no obvious organic cause. This paper discusses the nature of give-up-itis, with progressive demotivation and executive dysfunction that have clinical analogues suggesting frontal-subcortical circuit dysfunction particularly within the dorsolateral prefrontal and anterior cingulate circuits. It is hypothesised that progressive give-up-itis is consequent upon dopamine disequilibrium in these circuits, and a general theory for the cause and progression of give-up-itis is presented in which it is proposed that give-up-itis is the clinical expression of mental defeat; in particular, it is a pathology of a normal, passive coping response.

Introduction

The term ‘give-up-itis’ (GUI) was originally applied during the Korean war (1950–1953) to prisoners-of-war (PoW) who following severe trauma developed extreme apathy, gave up hope, relinquished the will to live and died, despite no obvious organic cause. One medical officer and PoW in Korea observed in some of his fellow captives symptoms he could assess without being able to describe them: a listlessness, a look, a turning from reality. When their symptoms appeared in various degrees and varying combinations he could estimate very closely how long a particular man he had come to know well would cling to life [1]. Another stated, ‘It was the feeling of many men, including some of the doctors who survived the experience, that some of the deaths were not warranted by a man’s physical condition. Instead, what appeared to happen was that some men became so apathetic that they ceased to care about their bodily needs. They retreated further into themselves, refused to get any exercise, and eventually lay down as if waiting to die. […] They seemed willing to accept the prospect of death rather than to continue fighting a severely frustrating and depriving environment’, and that this ‘fatal withdrawal’ was not simply a result of physical causes [2].

‘Give-up-itis' was carried forward to describe the same behaviour occurring in PoW camps in Vietnam, especially during 1964–1973, where one PoW, ‘…shuffled around the camp disconnected from the world around him […] he was really not with us. Finally, toward the end of September, he gave up, lay down, and died’ [3]. The term was later applied retrospectively to World War II camps in which deaths from a fatal withdrawal were described [4]. GUI was also reported in Nazi concentration camps where many victims died simply due to a loss of desire to live [5]. Elie Cohen [6] reports that, ‘At Ebensee I found a few times one or two men lying dead by my side in the morning. The evening before I had observed nothing in these people to show that their end was near’. Mary Lindell (in Ravensbrük camp) found that one of her friends, ‘…had given up and died, even though she had no organic illness’ [7].

GUI has also been observed by shipwreck survivors were trauma victims in life-rafts are reported to have given up and died from despair [8], e.g., ‘There were seven of us on the raft but the third officer died about two hours before we were picked up. He was very despondent and toward the end he lost heart and gave up and died’ (Bosun, 40 h liferaft, North Atlantic); ‘I think a number of the men became dispirited and despondent and it seemed to me they lost the will to live’ (Third Officer, 21 days lifeboat, 15 fatalities). Similarly, a medical officer who survived an aircraft crash reported, ‘On the next roll call he didn’t answer and I saw he had died. That scared me. There was nothing physically wrong with him. I wondered if it was going to be like this: one by one people would stop answering roll call. This was about five hours before rescue’ (personal debrief). Nor is GUI a recent phenomenon having been described in the early American Jamestown colony at various times between 1607 and 1625. Contemporary reports describe a, ‘…most strange Condition’ with colonists showing an inexplicable apathy, lethargy and indifference and, ‘…most give themselves over, and die of Melancholye’ [9]. A century later European slave-traders reported that captive slaves would give up hope and die ‘by the sulks’ [10].

Two factors stand out in cases of GUI: firstly, there appears to be no identifiable organic cause for a death which seems incomprehensible [11]. Death is psychogenic. For example, a medical officer during

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World War II describes a slightly wounded soldier who was brought to the hospital: 'He died – although his wound was of no importance and there seemed no other medical cause for his death' [12]; '…some of the deaths did not seem warranted by the physical conditions of the men,' [11]; one woman who had survived a Japanese prison camp in WWII noted, 'I feel very strongly that quite a number of people who died shouldn't have done so but they just gave up' [13]; a Soviet prisoner, after serving his sentence of 3650 days, was told that instead of release his term had been prolonged indefinitely and that same day he died, '… for no visible reason' [14]. Similarly in 17th Century Jamestown, '… people died who were not mortally ill', and that death, '…hath proceeded from a disease in itselfe not mortall', [9]. In more recent times the death of a hospital patient has been ascribed to psychogenic death following a surgical operation that he perceived to have been unsuccessful. It is reported that the day after the operation the patient showed the symptoms of regression, resignation, passivity and apathy and died within one day. The autopsy, histopathologic and toxicologic examinations showed no indications as to the cause of death [15]. In another case an active and conscientious 87-year old man one day took to his bed saying that he was going to die, which he did five days later. Clinically, his physician could find no specific cause of death (Dr Chris Brooks, personal communication).

A former inmate of Auschwitz concentration camp suggested that GUI seemed to be largely psychological in origin [16], a view which has been shared across the centuries: in 1620 George Thorpe in Jamestown reported, '…that more doe die here of disease of theire minde than of their body' [9]. Secondly, the lucidity and sanity of GUI victims is never in question and no observation of psychosis has ever been reported even up to death. When spoken to such people would respond rationally and appropriately, but would then revert to their previous state [11] suggesting that, despite the extremity of the situation, basic cognitive functions remain intact.

The key psychological factor in GUI appears to be a reactive syndrome following psychological trauma that includes extreme withdrawal from the environment, e.g. 'The first reaction of those arriving at the [concentration] camps was massive psychological shock that could last from a few days to several weeks. A few were not able to cope with this situation, gave up immediately, and died shortly after their arrival' [17]. Similarly, in a shipwreck incident, 'The men who died all became apathetic and their morale became very low' (Second Officer, lifeboat, North Atlantic). An examination of numerous accounts of GUI suggests that it is a gradual regression from normal, adaptive goal-directed behaviour through diminished executive function and demotivation to psychogenic death described variously as a 'slipping away', a 'passive suicide' with death coming by itself and the, '…gradual going out of a candle flame' [6]. One survivor of a shipwreck observed four others gradually dying, '…I had no thought people could die so easily. Their heads just fell back, the light seemed to go from their eyes, and it was all over' [18].

Hypothesis

It is proposed that 'give-up-itis' can be understood as a quantitative regression from normal, adaptive goal-directed behaviour that passes through a clinical spectrum from withdrawal, apathy, aboulia and psychic akinesia to psychogenic death. It is hypothesised that GUI behaviour occurs through frontal-subcortical circuit dysfunction, particularly within the dorsolateral prefrontal and anterior cingulate circuits, and is consequent upon dopamine disequilibrium within these circuits.

GUI pathogenesis

Give-up-itis follows a progressive psychological decline (see Fig. 1) that maps across the following five identifiable stages:

Stage I GUI: withdrawal and loss of initiative

The first stage of GUI has been most frequently reported following psychological trauma. The primary response is a psychological withdrawal and a docility coupled with a cessation of reflection and initiative. Victims have been described as showing a marked withdrawal of involvement from the current situation, accompanied by a paucity of emotion, listlessness, indifference and complete absorption and preoccupation with themselves [11]. In 16th Century Jamestown colonists' behaviour was described as a 'withdrawal from life' [9]; in the Korean camps it was a 'fatal withdrawal', and even refugees in safe Swiss camps were noted to become, '… a passive object of care… who vegetate' [19] and Viktor Frankl employs the same term to describe how the majority of the prisoners in Auschwitz would 'simply vegetate' [20].

Stage I GUI is characterised by a state of social withdrawal with diminished motivation, mood and initiative whilst consciousness and cognitive function remain normal. The individual is intrinsically capable of carrying out normal behaviours, but these are slower in initiation and shorter in duration than before. There is a dependency on others to structure activities and when spoken to these people respond rationally and appropriately but quickly return to their previous state [11]. Their speech and behaviour does not suggest psychiatric disorder which is consistent with the finding that withdrawal or demotivation is unrelated to a diminished level of consciousness, cognitive impairment or emotional distress [21].

It has been suggested that withdrawal from a traumatic situation can be a coping mechanism involving the constriction of overt behaviour and emotional responses although without any disintegration of the personality or the development of a psychosis. The victim is aware of his or her surroundings and what is going on but their own responses are sharply inhibited and suppressed [11]. Such inhibition can be seen as a form of protection which was evident in the Korean camps where the most common initial response was a physical and emotional withdrawal from the whole environment, coupled with an attitude of watching and waiting rather than hoping and planning [22]. However, if left unchecked, this detachment can progress to a reactive syndrome that includes apathy and more extreme withdrawal [23].

Stage II GUI: apathy

Exposure to extreme trauma, including survival of atomic bombing, PoW and concentration camps, has been reported to result in an 'apathetic syndrome' [23]. Frankl [20] noted in concentration camps that within, '… a few days the prisoner passed from the first to the second phase; the phase of relative apathy, in which he achieved a kind of emotional death'. An 'apathy reaction' was widely observed amongst PoWs [11] even extending to a profound apathy syndrome [24] and was experienced by one prisoner as a 'demoralising melancholia' [25], and by another as a 'colossal inertia' who stated, 'I remember waking each morning and being unable to get up. I was not tired – I was just apathetic [and] every act, every decision, required an effort out of all proportion to the circumstances' [12]. A similar recent account comes from an Englishman held in a Russian prison during 2003–5, 'Within a few days of our arrival, perhaps a week, a heavy melancholy descended on me. It was different and altogether bigger and more alarming than plain sadness or frustration or anger. It felt almost physical […] For hour upon hour I lay on my back staring listlessly at the ceiling, and soon the smallest task began to feel like the mightiest effort' [26]. Cochrane [12] described the psychopathology of camp trauma as consisting of 'the fate of apathy' and a degree of apathy was noted in every person at some time, the depth and duration of the state varying between individuals. In the camps prisoners are described as slipping into 'relative apathy' after the first stage of psychogenic trauma, taking no interest in their surroundings and ceasing to strive after self-preservation [6,20]; others describe a 'hopeless lassitude', a 'symbolic death' [13]. People in Stage II GUI are described as being dishevelled, dirty